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Electronic Supplementary Materials (ESI), Supporting Information

Selective glucose conversion to 5-hydroxymethylfurfural (5-HMF) instead of

levulinic acid with MIL-101Cr MOF-derivatives

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Materials

Reagents were purchased from the following distributors and used without further purification, except for THF which was distilled prior to use, to remove the stabilizer and except for the Amberlyst resin, which was dried at 110 °C before use.

Chromium(III) nitrate nonahydrate (99 %), terephthalic acid (99+ %), 2-nitroterephthalic acid (99+%) and 5-hydroxymethylfurfural (98%) from Acros Organics. *N*,*N*-Dimethylformamide (99.9 %), sulfuric acid (95%) from VWR. Methanol and ethanol (99.9 %) from Merck.

Monosodium 2-sulfoterephthalic acid (>98.0%) and levoglucosan (>99.0%) from TCI D-(+)-glucose, >99.5% (GC), cellulose (microcrystalline, powder) and levulinic acid (98%) from

Sigma Aldrich, D(+)-maltose (>95%) from Roth, Amberlyst-15(H), wet from Alfa Aesar.

Synthesis

All MIL-101Cr materials were synthesized hydrothermally, utilizing an autoclave and programmable oven for heating according to literature procedures.¹

<u>MIL-101Cr-NO₂ (MIL-NO₂</u>): CrO₃ (0.75 g, 7.5 mmol), H₂BDC-NO₂ (1.58 g, 7.5 mmol) and 12 mol/L HCl (1.1 g, 30 mmol) were dissolved in H₂O (30 mL), then transferred into a Teflon-lined stainless steel autoclave. This acidic solution was heated at 180 °C for 6 days (heating ramp 5 h; cooling ramp 15 h).

<u>MIL-101Cr-SO₃H(0.33)</u> (<u>MIL-SO₃H(0.33)</u>): CrO₃ (0.75 g, 7.5 mmol), H₂BDC-SO₃Na (1.00 g, 3.75 mmol), H₂BDC (0.62 g, 3.75 mmol) and 12 mol/ HCl (1.02 g, 28 mmol) were dissolved in H₂O (34 mL), then transferred into a Teflon-lined stainless steel autoclave. This acidic solution was heated at 180 °C for 6 days (heating ramp 5 h; cooling ramp 15 h).

<u>MIL-101Cr-NO₂/SO₃H (MIL-NO₂/SO₃H)</u>: CrO₃ (0.75 g, 7.5 mmol), H₂BDC-SO₃Na (1.00 g, 3.75 mmol), H₂BDC-NO₂ (0.79 g, 3.75 mmol) and 12 mol/L HCl (1.02 g, 28 mmol) were dissolved in H₂O (34 mL), then transferred into a Teflon-lined stainless steel autoclave. This acidic solution was heated at 180 °C for 6 days (heating ramp 5 h; cooling ramp 15 h).

<u>MIL-101Cr-SO₃H (MIL-SO₃H)</u>: CrO₃ (3.0 g, 30 mmol), H₂BDC-SO₃Na (6.00 g, 30 mmol) and 12 mol/L HCl (2.2 g, 60 mmol) were dissolved in H₂O (4x30 mL), then transferred into 4 Teflon-lined

stainless steel autoclaves. This acidic solution was heated at 180 °C for 6 days (heating ramp 5 h; cooling ramp 15 h).

Activation procedure for above MIL materials: The green solids were stirred overnight with 80 mL of H_2O . After the water washing procedure, the centrifuged product was stirred in 150 mL of ethanol at reflux overnight. The solid was centrifuged off, suspended in fresh ethanol (150 ml) and stirred at reflux for 3 days. The procedure was repeated again with 150 mL of fresh ethanol. Finally, the products were collected by centrifugation and dried at 110 °C overnight.

Yields <u>MIL-NO₂</u>: 1.06 g, 17 %, <u>MIL-SO₃H(0.33)</u>: 1.32 g, 21%, <u>MIL-SO₃H/NO₂:</u> 1.32 g, 20 %, <u>MIL-SO₃H</u>: 9.2 g, 32 %.

<u>MIL-101Cr</u>: Terephthalic acid (0.66 g, 4.0 mmol) was added to an aqueous solution of TMAOH (20 mL, 0.05 mol/L) and stirred for 10 min at room temperature. $Cr(NO_3)_3 \cdot 9H_2O$ (1.6 g, 4.0 mmol) was added and the mixture was stirred again for 20 min. The suspension was transferred into a Teflon-lined autoclave and was heated to 180 °C for 24 h (heating ramp 10 h; cooling ramp 18 h). Activation procedure: The green solid was washed (in the given order) with 90 mL H₂O, 90 mL DMF and 90 mL ethanol. After the water washing procedure, the centrifuged product was stirred in 90 mL DMF overnight at room temperature and then heated in the dispersion for 6 h at 110 °C. After cooling to room temperature the powder was centrifuged off and re-suspended in 90 mL ethanol. The mixture was stirred again at room temperature overnight and then heated for 2 d at 90 °C in ethanol. Finally, the products were collected by centrifugation and dried at 70 °C overnight Yield: 0.73 g 47 %.

For catalyst activation the materials were dried prior to each experiment at 140 °C for 15 h in air.

Characterization techniques

NMR spectra were measured on a Bruker Avance III – 600 and 300 and a Bruker Avance DRX 500 spectrometer. ¹H shifts were referenced to the deuterated solvent signals for CDCl₃ ¹H: δ = 7.26 ppm and for spectra in D₂O ¹H shifts were referenced to the signal of 3-(trimethylsilyl)propionic-2,2,3,3-d₄ acid sodium salt with δ = 0 ppm.

NMR reaction control experiments

The ratio between 5-HMF and levulinic acid was determined by ¹H NMR in CDCl₃. Also NMR spectra in D₂O have been measured, to identify all reaction products. All NMR spectra for determination of 5-HMF vs. levulinic acid were measured with D1 = 20 sec. If not stated otherwise the complete reaction solution was dried *in vacuo* and then dissolved in the deuterated solvent, without any workup.

The ratio of mixed linkers in <u>MIL-SO₃H(0.33)</u> and <u>MIL-SO₃H/NO₂</u> was determined by digestion of the MIL material in D₂O/NaOD. First the MIL (40 mg) was dissolved in 1 mL of D₂O with 0.15 mL of NaOD/D₂O (40%). To the resulting green solution HCl (conc.) was added adjusting the pH to 10-11. After separation of the main part of precipitated Cr(III)-hydroxide salts by centrifugation, the supernatant solution was measured. It was not possible to improve the quality of NMR spectra by precipitation and resolvation of the linker, because 2-sulfo-terephtalic acid is very good soluble in basic and acidic aqueous solution.

Catalytic conversion of glucose

Standard procedure

The MIL samples were dried at 140 °C for 15 h in air prior to each experiment. The catalytic experiments were conducted in Pyrex glass vials equipped with a cap and a stirrer. The accuracy of the MIL sample weight was 50±0.2 mg. Every experiment was performed at least in duplicate to ensure reproducibility. For every measurement point a new reaction had to be started due to the necessary work up procedure. From every reaction two samples were taken and each sample was measured with GC three times. From the resulting two values the average was taken.

Standard conditions: catalyst $5.22 \cdot 10^{-5}$ mol, glucose 223 mg (1.24 mmol), solvent 5 mL (THF/H₂O 39:1), 130 °C, 24 h.

MOF	Mass [mg] corresponding to 5.22·10 ⁻⁵ mol
MII-NO ₂	44.3
MIL- NO ₂ /SO ₃ H	46.9
MIL-SO ₃ H(0.33)	41
MIL-SO ₃ H	50
MII101Cr	37.4

For other MIL catalysts, the mass (mg) corresponding to $5.22 \cdot 10^{-5}$ mol was used:

Analysis of products

Gas chromatographic (GC) analyses were done with a GC-2014 Shimadzu instrument coupled with a flame ionization detector (FID) and a GC-MS Finnigan Trace DSQ with Finnigan Trace GC Ultra System. GC Parameters: Autosampler injection volume 1.0 μ L, rinses with solvent pre-run 2x, post-run 1x, rinses with sample 2x; injector temperature 240 °C; column information: Ultra 2 (Ø 0.2 mm x 25 m, 5%-Phenyl)-methylpolysiloxane), column maximum temperature: 320 °C; column oven program: start at 60 °C, hold time 0.30 min, heating 7 °C/min until 115 °C, hold time 1.0 min °C, heating 12°C/min until 200 °C, hold time 0.30 min. Total program time 16.54 min.

Concentrations of 5-HMF in the organic THF phase were quantified by GC with external standard calibration ($R^2 = 0.9991$, R = 0.9995). It was already shown that at least 93% of 5-HMF is present in the THF phase.² Phase separation has been achieved by extracting the reaction mixture with 5 mL saturated sodium chloride solution.

Conversion HMF = (moles of 5-HMF/moles of initial glucose loading) \cdot 100 as determined by GC. For the 5-HMF conversion only the yields detected by GC in the THF phase after workup are given in the main article.

Possible corrections for maximum yield: Since only 93% of 5-HMF is present in the THF phase (the rest remains in the H_2O phase),² the conversion will even be slightly higher. Another factor is the uptake of reaction mixture from MIL-SO₃H itself. Therefore, after the catalyst was separated and the supernatant removed, new THF was added to the catalyst. The mixture was stirred for 1 h and separated again by centrifugation. The supernatant THF solution was analyzed by GC again. After 24h reaction an additional 5-HMF yield of 1.3 % was found.

50 mg MIL-SO₃H (M = 956.7 g/mol) corresponds to $5.22 \cdot 10^{-5}$ mol, multiplied with three for each Cr atom in the {Cr₃} formula unit gives $1.57 \cdot 10^{-4}$ mol.

formula unit: [Cr₃(H₂O)₂(OH)O(O₂CC₆H₃(SO₃H)CO₂)₃]

The reference experiments with chromium(III) nitrate nonahydrate, Amberlyst 15 and sulfuric acid were conducted with $1.57 \cdot 10^{-4}$ mol.

Theoretical calculation of Brønsted acid sites of MIL-materials

For each mol of activated and dried MIL-101 formula unit of $[Cr_3(O)(OH)(bdc-X)_3(H_2O)_2]$ we assume a potential maximum of

2 mol of Brønsted acid sites for $X = NO_2$ (namely the two terminal H₂O ligands),

5 mol of Brønsted acid sites for $X = SO_3H$ (two terminal H₂O and three SO₃H),

2.99 mol of Brønsted acid sites for $X = SO_3H(0.33)$ (two terminal H₂O and 3x0.33 SO₃H),

3.5 mol of Brønsted acid sites for $X = NO_2(0.5)/SO_3H(0.5)$ (two terminal H₂O and 3x0.5 SO₃H)

Compound	Retention time [min]	Compound
THF	1.03	
HMF	6.97	HO
Levulinic acid	4.5	HOHO

Table S1 Retention times of reagents and products in GC measurement

Filtration test

After running the catalytic glucose to 5-HMF reaction for the chosen time, the mixture was cooled to 0 °C and the catalyst was separated by centrifugation. The clear supernatant solution was filtered with a syringe filter of the type RC 0.2 μ m. The reaction was continued with the filtrate in a new reaction vial under identical reaction conditions for at least 18:45 h. Then the standard workup procedure was performed and the filtrate was analyzed by GC.

Recycling test

For experiments with multiple runs each catalytic reaction was run for 24 h, stopped by cooling to 0 °C and centrifuged until the supernatant solution was visibly clear (10 min). With the clear solution the standard workup procedure was performed and a sample for GC analysis was collected. The catalyst was washed one time with THF (4 ml) and dried at 140°C for ca. 2 h in vacuum. After that a new reaction was started under the standard conditions stated above. This procedure was repeated for 3 to 4 runs, after which PXRD and nitrogen sorption analysis was measured.

In a second set of experiments the conversion was determined following the same procedure, but implement further washing steps with water and ethanol. Additionally, it was tried to reactivate the material by stirring in hydrochloric acid. After the treatment with acid the solution has been washed with water until a neutral pH was achieved in the filtrate.

Structural elements of MIL-101Cr

pentagonal windows and hexagonal windows as largest windows in cages:



Figure S1 Building blocks for MIL-101, $[Cr_3(\mu_3-O)(F,OH)(BDC)_3(H_2O)_2]$, generated from the deposited X-ray data file at the Cambridge Structure Database (CSD-Refcode OCUNAK)³ using the program DIAMOND.⁴ Trinuclear { $Cr_3(\mu_3-O)(F,OH)(H_2O)_2(O_2C-)_6$ } building units and bridging benzene-1,4-dicarboxylate ligands form pentagonal and hexagonal rings (a) which are assembled into mesoporous cages. b) The yellow spheres in the mesoporous cages with diameters of 29 or 34 Å, respectively, take into account the van-der-Waals radii of the framework walls (water-guest molecules are not shown). The different objects in this figure are not drawn to scale.

NMR spectra of digested MILs



.4 9.2 9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 f1(ppm)

Figure S2 ¹H NMR spectra (300 MHz) after digestion of MILs in D₂O/NaOD. a) MIL-NO₂, b) MIL-NO₂/SO₃H, c) MIL-SO₃H(0.33) (*artefact signal from solvent) and d) MIL-SO₃H. Slight shifts in different spectra a *versus* b and c versus d were induced by residual paramgnetic Cr^{3+} species.

Scanning electron microscopy (SEM)



Figure S3 Scanning electron microscopy images of a) MIL-NO₂, b) MIL-NO₂/SO₃H, c) MIL-SO₃H(0.33) and d) MIL-SO₃H.





Figure S4 Powder X-ray diffractograms of MIL-NO₂, MIL-NO₂/SO₃H, MIL-SO₃H(0.33) and MIL-SO₃H. Measured for 2 h.

Nitrogen sorption isotherms



Figure S5 Nitrogen sorption isotherms of MIL-NO₂, MIL-NO₂/SO₃H, MIL-SO₃H(0.33) and MIL-SO₃H. Filled symbols are for adsorption, empty symbols are for desorption.



Figure S6 Photographic images of a) pure MIL-SO₃H powder; b) MIL-SO₃H after 24 h catalysis under standard conditions with THF:H₂O (v:v) 39:1; c) MIL-SO₃H after catalysis in THF:H₂O (v:v) 4:1 c) d) reacted in EtOH/H₂O.



Figure S7 Nitrogen sorption isotherms of MIL-SO₃H after the catalytic reaction under standard conditions for 24 h in EtOH/H₂O 39:1, THF/EtOH/H₂O (23:16:1) and before catalysis.

Table S2 Weights of different catalytic materials together with insoluble humins after the reaction (24 h, 130 °C, 50 mg catalyst (or $4.7 \cdot 10^{-4}$ mol for H₂SO₄ and Cr(NO₃)₃). Samples have been dried at 120 °C overnight.

Catalytic material	Weight of insoluble material
	after catalytic reaction [mg]
MIL-SO ₃ H	91
MIL-SO ₃ H with substrate levoglucosan	85
MIL-SO ₃ H after 3 runs	72
H_2SO_4	70
Cr(NO ₃) ₃	132
MIL-SO ₃ H in EtOH/H ₂ O	53

Table S3	Multiple	run experiment	s with N	AIL-SO ₃ H
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Run number	Yield of 5-HMF [%] ^a
1	29
2	24
3	19
4	13
With washing steps	
2	18
3	16

a) Determined by GC.

NMR data of reaction products from catalytic substrate conversion





Figure S8 ¹H NMR data of the reaction products of

a) MIL-SO₃H with levoglucosan (conditions: levoglucosan 1.24 mmol, MIL-SO₃H $5.22 \cdot 10^{-5}$ mol, THF/H₂O 5mL, (v:v) 39:1, 130 °C, 24 h), spectrum in D₂O;

b) MIL-SO₃H with fructose (conditions: fructose 1.24 mmol MIL-SO₃H $5.22 \cdot 10^{-5}$ mol, THF/H₂O 5 mL, (v:v) 39:1, 130 °C, 24 h), spectrum in CDCl₃;

c) MIL-NO₂ with glucose (conditions: glucose (1.24 mmol), MIL-NO₂ $5.22 \cdot 10^{-5}$ mol, THF/H₂O 5mL, (v:v) 39:1, 130 °C, 24 h), spectrum in D₂O;

d) MIL-SO₃H with glucose reacted at 100 °C (conditions: glucose 1.24 mmol, MIL-SO₃H $5.22 \cdot 10^{-5}$ mol, THF/H₂O 5mL, (v:v) 39:1, 100 °C, 24 h), spectrum in D₂O.



Figure S9 a) MIL-SO₃H with glucose after 8 h (conditions: glucose 223 mg, MIL-SO₃H $5.22 \cdot 10^{-5}$ mol, TF/H₂O 5ml, 39:1, 130°C, 8 h), spectrum in D₂O; b) MIL-SO₃H with glucose after 15 h (conditions: glucose 223 mg, MIL-SO₃H $5.22 \cdot 10^{-5}$ mol, THF/H₂O 5ml, 39:1, 130°C, 15 h), spectrum in D₂O.



Figure S10 ¹H NMR of the reaction solution of a) H_2SO_4 and b) Amberlyst-15 with glucose. Conditions: glucose 223 mg, THF/H₂O 5 mL (v:v 39:1), 130 °C, 24 h. For H₂SO₄ and Amberlyst-15 reaction was conducted with 1.57 · 10⁻⁴ mol each. Spectra in D₂O.



Figure S11 ¹H NMR spectra of the reaction solution of a) 5-HMF with MIL-SO₃H (conditions 5-HMF 1.03 mmol, MIL-SO₃H 5.22·10⁻⁵mol, THF/H₂O 5 ml (39:1), 130 °C, 24 h), spectrum in D₂O b) glucose with MIL-SO₃H, only the THF phase after workup procedure (conditions: MIL-SO₃H 5.22·10⁻⁵mol, glucose 223 mg, THF/H₂O 5 ml (39:1), 130 °C, 24 h), spectrum in CDCl₃. Normally the whole THF/H₂O solution was used for NMR (after centrifugation of the MIL catalyst). Here, it was seen that the 5-HMF to levulinic acid ratio is higher as workup leaves the latter partly in the aqueous phase.

Potentiometric titration experiments

Potentiometric titration experiments were conducted with a Titrino plus 848 (Metrohm). Dynamic equivalence point titration was used. Program details for experiments using sodium chloride as exchange agent (backtitration): dynamic equivalence point titration, signal drift 1 mV/min, waiting time minimum 10 sec, maximum 300 s, temperature 21 °C.

Equivalence points have been determined by maxima of ERC value (Equivalence point recognition criterion), which uses the first derivative of the titration curve. Titrations were performed at least in a triplicate and with varying concentrations of MIL-MOF and NaOH.

Program details for experiments with using sodium nitrate as exchange agent (backtitration): dosing rate 0.2 mL/min, signal drift 30 mV/min, minimum increment 0.05 mL, maximum increment 0.2 mL; temperature 21 °C.

Experiment using NaCl as exchange agent

The acidity of MIL-materials has been determined by acid-base backtitration using NaCl as ion exchange agent. For direct titration with MOFs no equilibrium of values could be found, also not after adding very small amounts of base (50 μ L) and long waiting times (5 min). The results of experiments were not reproducible. Besides, MIL materials are known to decompose in basic milieu and it cannot be sure at which pH this process starts. For this reason backtitration method was used. Based on literature procedures,⁵ in a typical experiment 50 mg or 100 mg of MOF was suspended in saturated NaCl aqueous solution (10 mL). The mixture was stirred for 20 h, centrifugated and washed with 10 mL of water (stirring time 20 min.). The filtrate was titrated with NaOH with a concentration of 0.001 mol/L or 0.005 mol/L. For all solutions Millipore water was used, additionally the solutions have been treated in an ultrasonic bath and with gaseous nitrogen. The saturated NaCl solution was heated and cooled to room temperature under inert atmosphere to minimize carbon dioxide in solution.



Figure S12 Titration of MIL-X with NaOH (different concentrations)

The titration curve of MIL-SO₃H shows 2 steps which is unexpected, since there should be only one kind of acidic protons. Therefore reference titrations have been performed. First only the pure saturated NaCl solution was titrated (Fig. S13). As expected the pH rises immediately very fast.



Figure S13 Reference experiments of NaCl pure without catalyst with 0.001 M and 0.005M NaOH solution.

It was taken into account, that the unexpected behavior can originate from leaching of the linker 2-sulfoterephtalate or chromium metal ions into solution). Titration of both 2-sulfoterephtalate (5 mg, $2.0 \cdot 10^{-5}$ mol) or chromium nitrate ($1.57 \cdot 10^{-4}$ mol in 25 ml H₂O) with 0.005 M NaOH shows that the linker is a strong acid whereas chromium nitrate is a weak acid. The strong rise in pH at a volume of ca. 90 ml is coming from insoluble chromium hydroxide which precipitated from the solution.



Figure S14 Titration of a) 2-sulfoterephtalic acid and b) chromium nitrate in NaCl/H₂O with 0.005 M NaOH.

Assuming linker leaching from linkers inside the pores, which are not coordinated to metal, it can be proposed that the surface area should be enhanced after washing with NaCl. Therefore MIL-SO₃H (50 mg) was stirred in saturated NaCl for 20 h. Then the MOF was washed three times with water (40 mL each). From N₂ sorption experiments it could be shown that the surface area decreased to 1040 m²/g.

If the acidity is coming from leaching of residual linkers or chromium nitrate, those should also leach in pure water, since both are good soluble in water. Therefore MIL-SO₃H (50 mg) was stirred for 20 h in pure water, and after centrifugation the solution was backtitrated with NaOH (0.005 M) (Figure S15). The pH of the solution rises immediately and a behavior similar to pure NaCl/H₂O solution was found. No leaching occurs.



Figure S15 a) MIL-SO₃H (50 mg) stirred in pure water, centrifuged and titrated back with 0.005 M NaOH, b) N_2 sorption isotherme of MIL-SO₃H stirred in saturated NaCl solution for 20 h, centrifugated and washed 3 times with water.

In conclusion, it can be proposed, that saturated NaCl solution gives rise to partial decomposition of MIL catalyst and is not suitable for the determination of acidity.

Experiment using NaNO3 as exchange agent

Since it was concluded that sodium chloride is not suitable for determination of acidic sites, according to a modified procedure following the work of R. C. Klet *et al.* titration was repeated using sodium nitrate (0.01 M).⁶ For direct titration with MOFs no equilibrium of values could be found, also not after adding very small amounts of base (50 μ L) and long waiting times (5 min). The results of experiments were not reproducible. Besides, MIL materials are known to decompose in basic milieu and it cannot be sure at which pH this process starts. For this reason backtitration method was used.

In a typical experiment 50 mg of MIL was suspended in NaNO₃ aqueous solution (0.01 M, 40 mL). The mixture was stirred for 20 h, centrifugated and the filtrate was titrated with NaOH with a concentration of 0.001 mol/L or 0.005 mol/L. For all solutions Millipore water was used.



Fig. S16 Titration of MIL-X, using NaNO₃ (0.001M), backtitration method.

Taking the largest maximum into account, the molar fraction was calculated (Table S3). When two titrations were performed the values have been averaged.

Table S4	Amount of acid sites,	determined by	potentiometric titration	with NaOH (0	.001 mol/L)
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MIL-X	Volume ^a [ml]	mmol H ⁺ (for 50 mg MIL)	Mol H ⁺ /mol MIL	Calc. value mol H ⁺ /mol MIL	Amount %
MIL-SO ₃ H ^b	4.52	0.023	0.43	5	8.6%
MIL-SO ₃ H(0.33)	17.45	0.017	0.28	3	9.3%
MIL-NO ₂ /SO ₃ H	4.21	0.004	0.076	3.5	2.2%
MIL-NO ₂	6.76	0.007	0.12	2	6%

^a volume for highest maximum in first derivative curve. ^b NaOH 0.005 mol/L was used.

Since the results from experiments are not really reproducible and remained inconclusive, our attempts are documented here, but not discussed further.

Mechanistic aspects of 5-HMF formation from glucose

Several pathways for the formation of 5-HMF from glucose are under discussion and especially for porous heterogeneous systems it is very difficult to elucidate exact mechanisms. Therefore a brief overview over recent insights in 5-HMF formation from glucose is given here (Fig. 8, cf. Fig. 2). The Brønsted base catalyzed glucose isomerization to fructose followed by the Brønsted acid catalyzed glucose dehydration to 5-HMF and a tandem Lewis/ Brønsted acid route have been discussed recently.^{7,8,9} Although all these studies refer to aqueous homogeneous systems, valuable information can be gained. Thiel and coworkers developed criteria for good metal catalysts in the glucose to fructose isomerization and identified Cr(III) and Al(III) as best candidates. One of the most important criteria is moderate Lewis and Brønsted acidity ($pK_a = 4-6$).^{9b} Detailed kinetic studies using Cr(III)-salts led to the conclusion that the Brønsted acidity of metal-aqua complexes has significant impact on glucose conversion.^{9c} [Cr(H₂O)₅OH]²⁺ has been identified as the most active Cr-species in glucose to fructose isomerization; aqua ligands are displaced by glucose to enable ring-opening and isomerization (Fig. S17b).^{9c} Recently, Vlachos and coworker showed that in the aqueous CrCl₃-HCl system adjusting the concentration of both CrCl₃ and HCl has a higher influence on 5-HMF yield than the change of temperature or CrCl₃ concentration. The rate limiting step can change from fructose dehydration to glucose isomerization with an increase of Brønsted acid concentration.^{9a}

Following the model of only Brønsted acid conversion of glucose, the first step is the protonation of hydroxyl groups and in consequence, the rate limiting step involves this first dehydration (Fig. S17a). Vlachos and coworker conclude from experimental and theoretical data that also the direct dehydration to levulinic acid and formic acid without 5-HMF formation is possible. Besides they identified two intermediate species composed of five-membered rings. Their study further confirms the strong dependence of dehydration rate on temperature and pH and suggests a reaction mechanism via a cyclic intermediate (Fig. S17a).⁸

An important difference is the reaction time scale, whereas conversion involving Lewis acid formation of fructose and dehydration to 5-HMF (Fig. S17b) is fast, in comparison to purely Brønsted acid dehydration which is slow.^{8,9a,10} Very recently Huber *et al.* presented a new mechanism for Brønsted acid dehydration of cellulose and glucose involving the intermediate Levoglucosan (Fig. S17c).¹¹

Having a closer look to heterogeneous catalyst systems, especially Sn-Beta zeolite has been investigated for the formation of 5-HMF from glucose.¹² From deuterium labeling experiments at the C2 position of glucose it was suggested that a hydrogen shift from the C2 to C1 positions is the rate-limiting step. In consequence a Lewis acid isomerization to fructose and Brønsted acid dehydration was postulated (Fig. S17b). In more detail it was proposed, that the OH group at the Sn-site lowers the energy barrier for the initial deprotonation step, which in turns activates the following Lewis acid catalyzed intramolecular hydride shift.^{12d}



Figure S17 Possible reaction pathways and intermediates for glucose to 5-HMF conversion.^{8,11,12}

Now all these findings should be interpreted taking the present MIL catalyst system into account.

Most importantly the mechanism of 1,2-hydrogen shift includes two neighboring open metal sites, which can coordinate to the oxygen atoms of glucose.^{12d} This is not conceivable from the MIL-101Cr structure (Fig. 3). Defect formation in MIL-101Cr leading to cis-open metal sites which is in principle conceivable, is not reported in literature.

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