Supporting information for

Mechanistic Insights into Metal-Lewis Acid Mediated Catalytic Transfer Hydrogenation of Furfural to 2-Methylfuran

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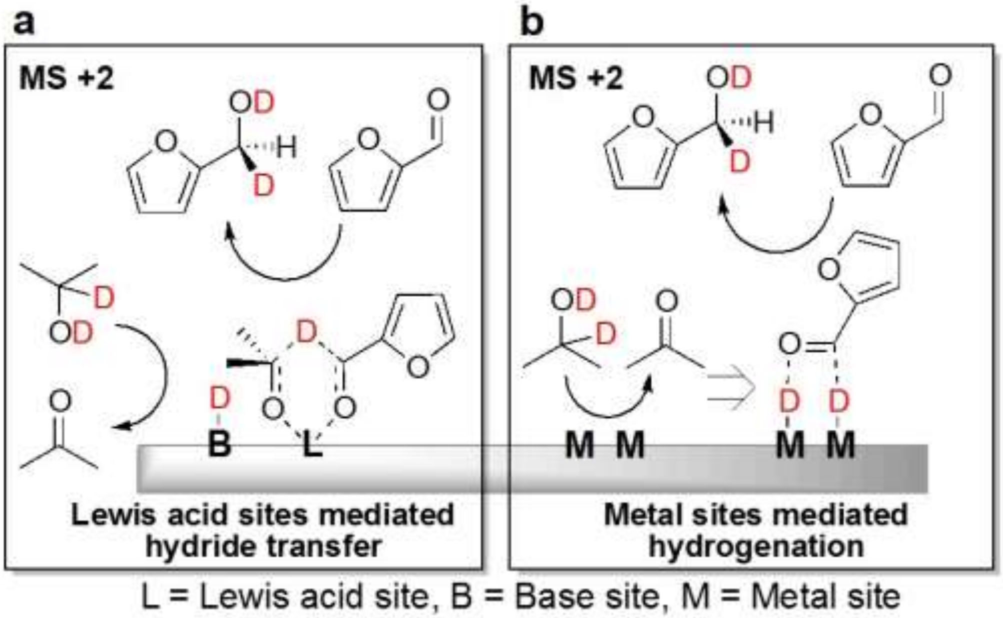
Hydrogenation mechanisms



Scheme S1. Furfural hydrogenation via a (a) Lewis acid site-mediated MPV, and (b) metal-mediated pathway. Both mechanisms result in FA with 2 Ds.

The Lewis acid-mediated MPV reaction cannot be distinguished from metal-mediated hydrogenation by replacing 2-propanol-d_0 with 2-propanol-d_8 (Scheme S1). In the MPV reaction, one D is transferred in one concerted step to furfural (Scheme S1a), and an additional D is added to the adjacent oxygen, forming FA-d_2 (MS +2, or 2 amu shift in the parent ion), where the 2 Ds are incorporated in the hydroxymethyl group. Although different mechanistically, the metal-mediated hydrogenation proceeds by adding adsorbed Ds across the carbonyl in furfural, forming the identical, isotopically labeled FA-d_2 (MS +2) molecule (Scheme S1b) as that formed from the MPV reaction. Thus, mass fragmentation analysis cannot differentiate the two mechanisms since the same molecule is formed from 2-propanol-d_8 regardless of the mechanism.

Confirming H/D exchange of 2-propanol-d_8 in the column gas chromatograph (GC)

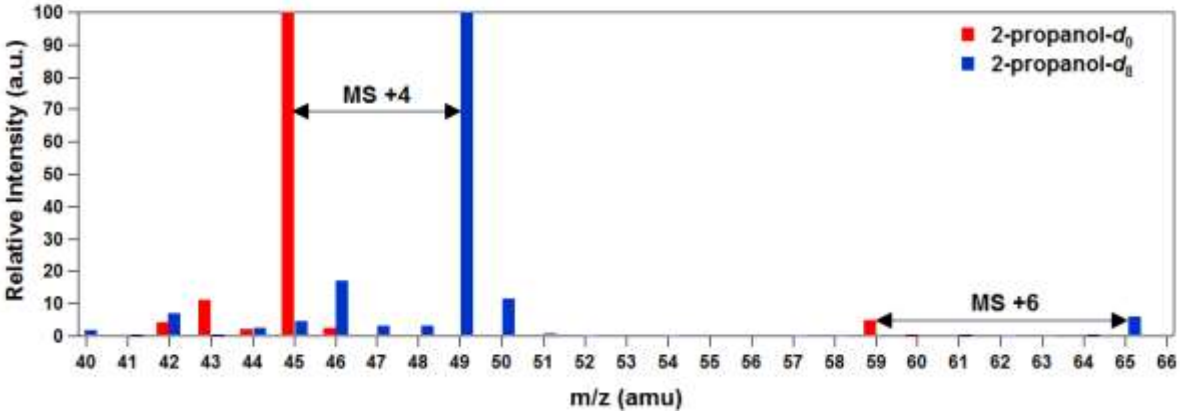
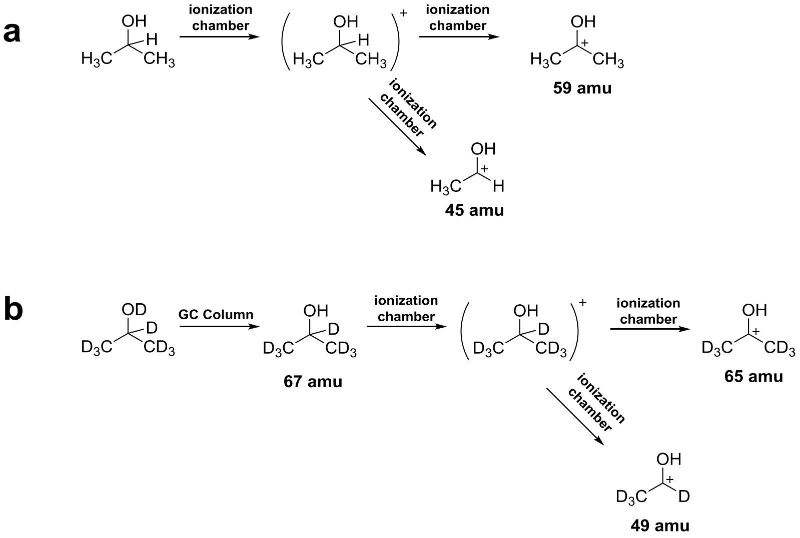


Figure S1. Mass spectrum of neat 2-propanol-d_8 versus 2-propanol-d_0 (NIST database).

The fragmentation pattern of neat 2-propanol-d_8 confirms the existence of facile H/D exchange of hydroxyl –OD groups to –OH groups in the GC column. The measured fragmentation pattern of 2-propanol-d_0 is in excellent agreement with the NIST database[1]. The parent ion of 2-propanol-d_0 (60 amu) shows ~0% abundance in the mass spectrum due to C-H bond cleavage at the β-C position in the ionization chamber (Scheme S2a), leaving $(CH_3COHCH_3)^+$ (Figure S1, 59 amu – red bars), which is consistent with the mass spectra of other *sec*-alcohols[2]. Similarly, the parent ion of 2-propanol-d_8 (68



Scheme S2. Scheme of the mass fragmentation of (a) 2-propanol in the ionization chamber of the GCMS and (b) 2-propanol-d_8 in both the GC and ionization chamber of GCMS yielding characteristic fragments observed.

amu) shows ~0% abundance; rather than the expected 66 amu signal, a signal at 65 amu was observed. This is attributed to the H/D exchange between the hydroxyl D in 2-propanol-d_8 and hydroxyl H in the GC column, forming $CD_3CDOHCD_3$ (Scheme S2b). Thus, following the ionization mechanism of *sec*-alcohols described above, the preferential cleavage of the C-D bond at the β-C position proceeds in the ionization chamber, leaving a $(CD_3CODCD_3)^+$ fragment, corresponding to 65 amu. Fast H/D exchange in the column is further evidenced by analysis of the highest intensity peaks (Figure S1, 45 amu – red bars and 49 amu – blue bars). The highest intensity peak in 2-propanol-d_0 (red bars, 45 amu) is due to the loss of CH_3 to form $(CH_3CHOH)^+$ (Scheme S2A). The 2-propanol-d_7 formed after H/D exchange at the hydroxyl group proceeds via the similar cleavage of the $–CD_3$ group to form $(CD_3CDOH)^+$ with an m/z of 49 amu. The existence of this fragment is only possible by H/D exchange of hydroxyl groups in the GC.

H/D exchange between t-butanol and adsorbed D

The 2-MF spectrum after FA hydrogenolysis with 2-propanol-d_8 in the solvent of t-butanol demonstrates that H/D exchange occurs very rapidly between the adsorbed D and the OH group of t-butanol, which is a key assumption in the interpretation of the FA spectrum in the hydrogenation of furfural. Mass fragmentation pattern analysis of 2-MF after reaction of FA and 2-propanol-d_8 in t-butanol shows only a small increase in the 83 amu signal as compared to the case when 2-propanol-d_0 was used as the hydrogen source (relative intensity of 83 amu signal increases from 4.8 to 14.0, Figure S2), suggesting that a small amount of D is incorporated into 2-MF even when 2-propanol-d_8 was used. This is in stark contrast to the case when hydrogenolysis of FA with 2-propanol-d_8 was carried out in the solvent of toluene (relative intensity of 83 amu signal increases from 4.8 to 60.8, Figure 1b), which suggests the majority of the surface adsorbed D in the presence of t-butanol is lost but not with toluene. This is

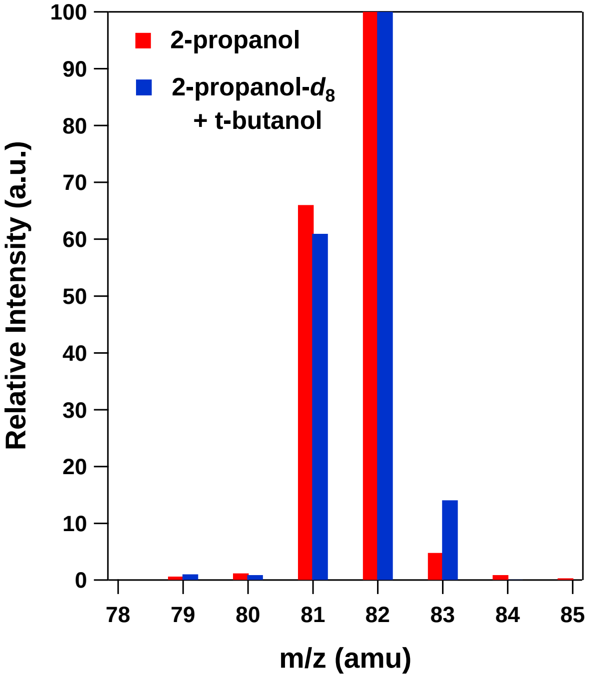


Figure S2. Mass spectrum of 2-MF obtained after FA hydrogenolysis with 2-propanol-d_0 and 2-propanol-d_8 in t-butanol solvent. Red bars: Before reaction; Blue bars: After reaction. Experimental conditions: 1 wt.% FA in 10% 2-propanol-d_8 in t-butanol solution; C_{cat}=4.1 g L^{-1}; 2.04 MPa N_2, T=140 °C and reaction time 5 h.

attributed to the exchange between D_{ad} and OH in t-butanol to form H_{ad} and D before the hydrogenolysis reaction occurs (Figure 1e). Since t-butanol, as the solvent, is in overwhelming excess, the majority of D_{ad} will be exchanged into H_{ad}. The small but still detectable degree of D incorporation in 2-MF in t-butanol can be explained by the fact that D accounts for about ~15% of the total active H/D pool. This calculation is based on the relative amounts of t-butanol and 2-propanol-d_8 in solution, 21.6 mL and 2.4 mL, respectively. On molar basis, this implies that 12% of hydroxyl groups in solution have a D rather than an H. Furthermore, since 2-propanol-d_8 conversion to acetone is relatively low, only a small fraction of β-D atoms are contained in the active exchange pool when dehydrogenated onto the surface (~15%). Thus, assuming the H/D exchange achieves equilibrium, the surface adsorbed H/D contains 15% D and 85% H, which lead to a minor degree of D incorporation of D in 2-MF. The significant degree of D incorporation into 2-MF in toluene is due to the lack of active hydrogen in toluene to exchange with D_{ad}.

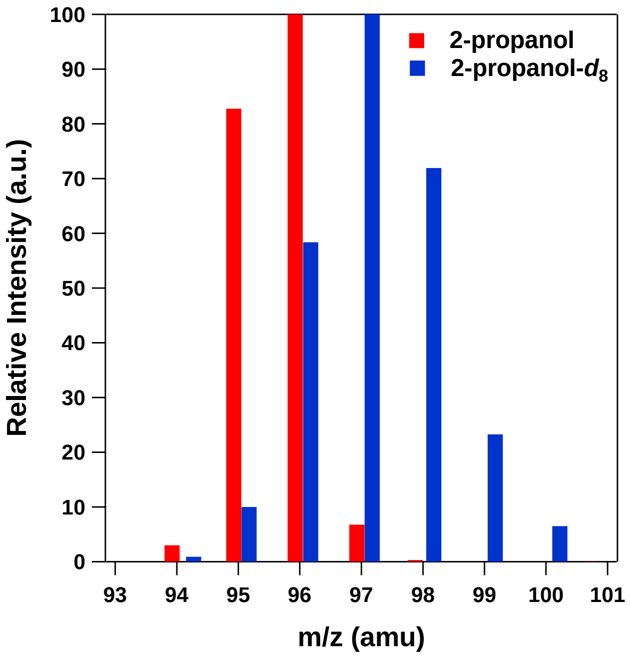
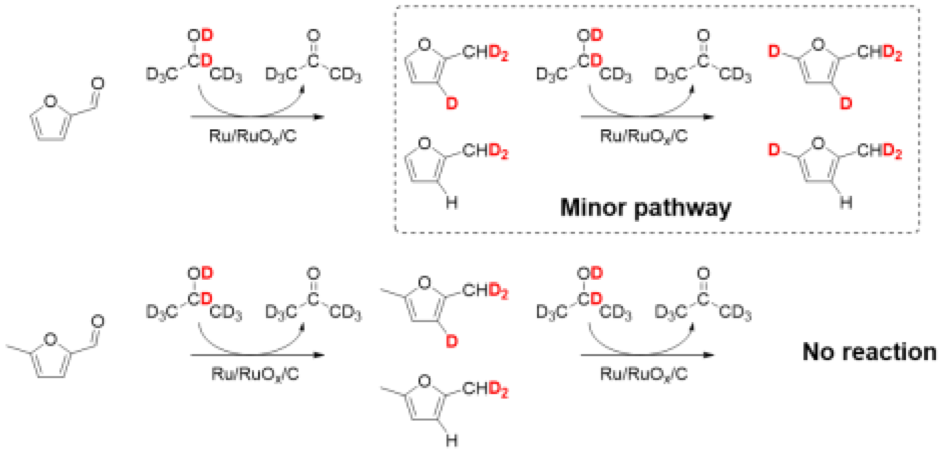


Figure S3. Mass spectrum of 2,5-DMF obtained after 5-methylfurfural hydrogenolysis. Red bars: Before reaction; Blue bars: After reaction. Experimental conditions: 1 wt.% 5-Methylfurfural in 10% 2-propanol-d_8 in toluene solution; C_{cat}=4.1 g L^{-1}; 2.04 MPa N_2, T=140 °C and reaction time 8.5 h.

Insignificance of H/D exchange via experiments with 5-methylfurfural



Scheme S3. H/D exchange at C_5 position of (a) MF (minor) and (b) 2,5-dimethylfuran (does not occur).

While H/D exchange is known to occur readily at the C_5 position in MF[3], experiments with 5-methylfurfural confirm the existence of a ring activated pathway in -OH bond scission. We have shown that H/D exchange occurs on C_5-H in MF in the presence of 2-propanol-d_8 under reaction condition[3], which suggests the possibility that the D incorporation might not be a direct result of the ring activated pathway, but rather, of H/D exchange in MF after reaction (Scheme S3). To clarify this point, we conducted reaction between 5-methylfurfural and 2-propanol-d_8 under identical reaction conditions (Scheme S3). As a result, a mass shift of the parent ion of 2,5-dimethylfuran (DMF) up to 3 amu (99 amu) was observed (Figure S3). Since a hydrogen is replaced by a methyl group on C_5 in DMF, no H/D exchange can occur[3], and thus the observed shifts are entirely due to the hydrogenolysis pathway via the furan ring activation described above. The similarity in the mass shifts of parent ions of MF and DMF in Figures 1b and S3, respectively, demonstrates the H/D exchange is an insignificant pathway for D incorporation in MF.

Additional evidence of ring activation via furfural-d_3 as starting material

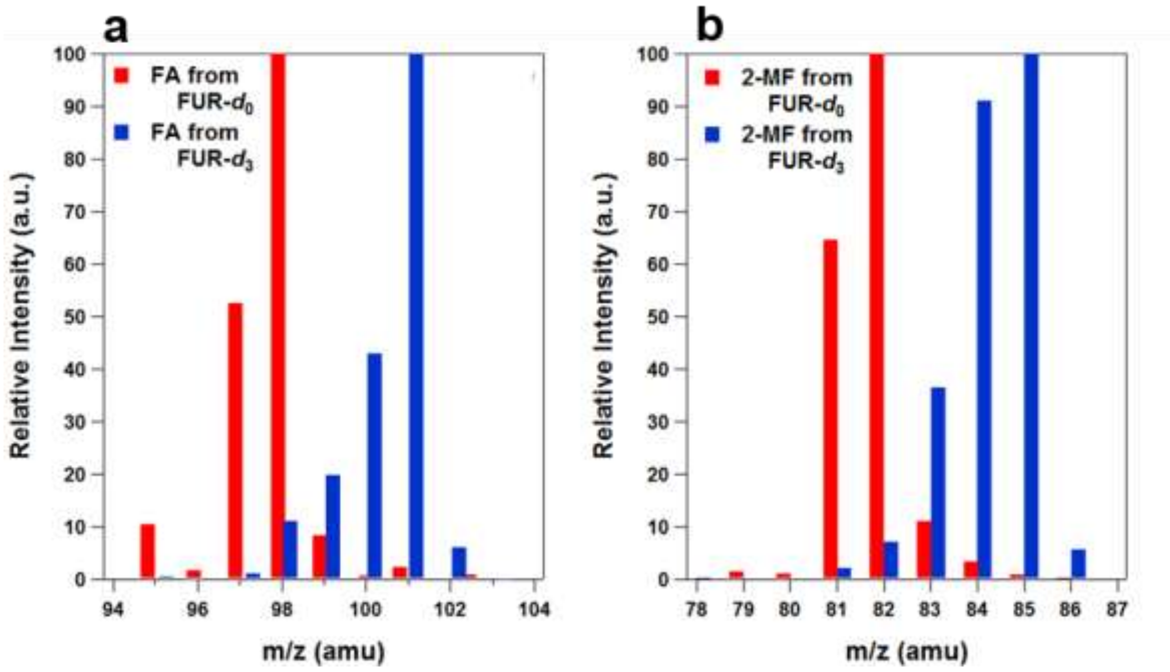
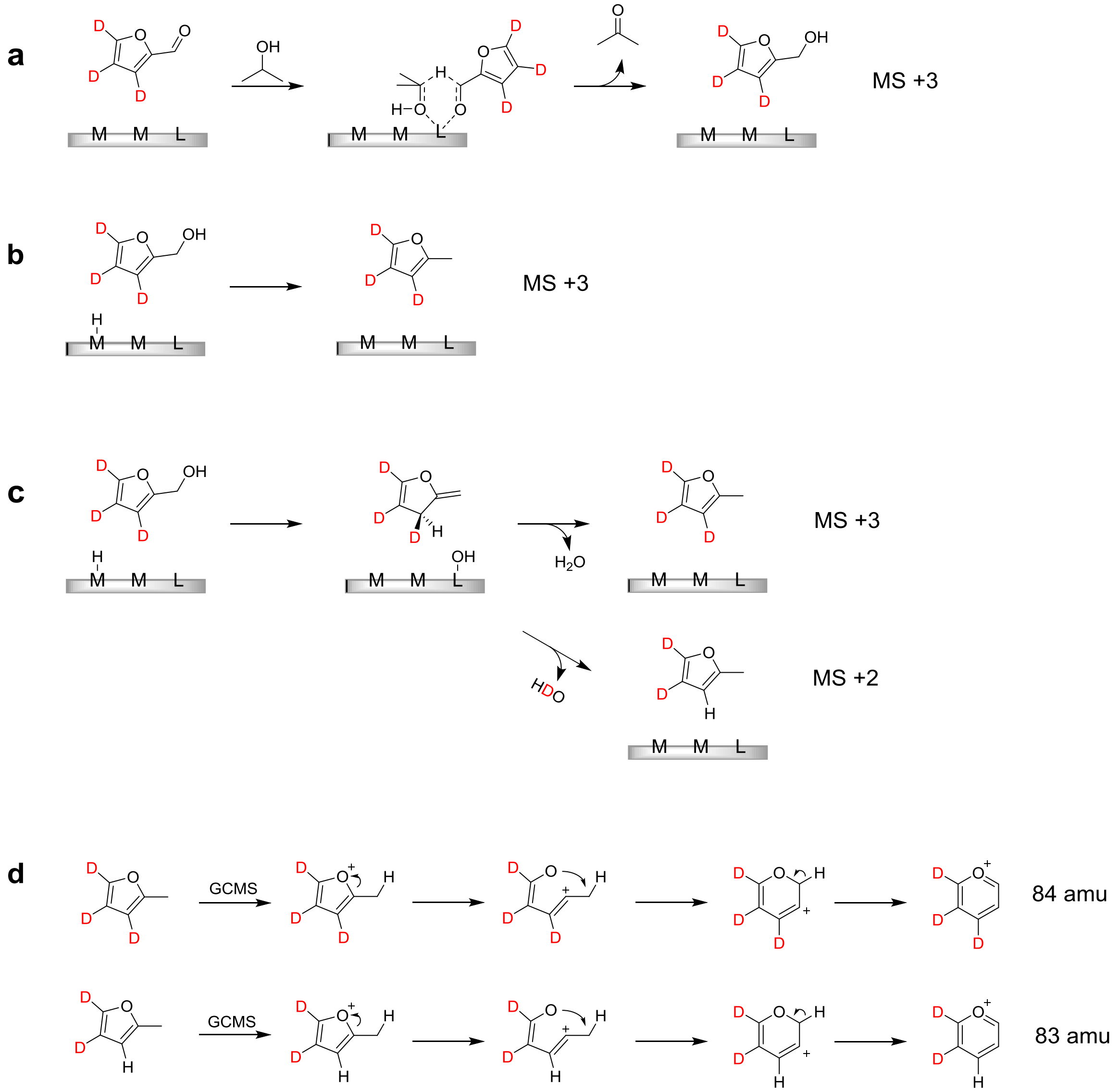


Figure S4. Mass spectra of (a) FA and (b) 2-MF obtained after furfural or furfural-d_3 hydrogenolysis. Experimental conditions: 1 wt.% furfural or furfural-d_3 in 10% 2-propanol-d_0 in toluene solution; C_{cat}=4.1 g L^{-1}; 2.04 MPa N_2, T=140 °C and reaction time 8.5 h. The most intense peak is scaled to 100%.

Evidence of ring activation is further demonstrated by the reaction of furfural-d_3 with 2-propanol-d_0, where furfural-d_3 contains 3 Ds at the 3 unprotected carbon atoms in the furan ring. The proposed mechanism outlined above would predict a +3 amu shift for FA formed from furfural-d_3 (Scheme S4a). In addition, the direct hydrogenolysis of FA-d_3 will result in MF containing 3 Ds, thus with a mass shift of 3 amu (Scheme S4b). Alternatively, hydrogenolysis of FA-d_3 via ring activation will lead to a mixture of MF with 2 and 3 Ds since the hydrogen source in this case in undeuterated 2-propanol (which lead to H_{ad} rather than D_{ad}, Scheme S4c). The mass fragmentation pattern of FA formed from the reaction of furfural-d_3 and 2-propanol-d_0 (blue bars in Figure S4a) shows a 3 amu shift from FA-d_0 (red bars in Figure S4a), which is consistent with the aforementioned mechanism. The small signal at 99 amu is likely due to the isotopic impurity of the furfural-d_3 sample (95%). 82 amu is the parent ion of MF-d_0, and the small 83 amu signal could be attributed to the natural abundance of ^{13}C. The 81 amu signal originates from the ionization induced structural rearrangement of cations to a 6-membered ring (Scheme S4d)[4], which does not result in the breaking of a C-H bond for C_3, C_4, or C_5. Thus MF-d_3 (with C_3, C_4 and C_5 bonded to D) is expected to have the same ratio between 84 amu and 85 amu as the ratio between 81 amu and 82 amu for MF-d_o (0.66). However, a significantly higher 84/85 ratio (0.91) was observed for the MF formed when furfural-d_3 is used as the reactant, suggesting the MF formed is not pure MF-d_3. Moreover, since there is no 80 amu signal for MF-d_0 (parent ion -2 amu), no 83 amu signal is expected in MF-d_3 (also parent ion -



Scheme S4. Mechanism demonstrating the production of all significant species of 2-MF after reaction between furfural-d_3 and 2-propanol where pathway (A) shows the formation of FA from furfural-d_8 indicating a mass shift of +3 amu, (B) shows the direct hydrogenolysis pathway from FA to 2-MF, indicating a mass shift of up to +3 amu, (C) shows the ring activated pathway from FA to 2-MF, indicating mass shifts of +3 amu (top) and +2 amu (bottom), and (D) shows the fragmentation of 2-MF in the ionization chamber of the GCMS, showing formation of 6-membered ring cations of mass 84 amu (top) and 83 amu (bottom).

2 amu). The fact that a substantial 83 amu signal (36.4%) appeared for MF formed from reaction between furfural-d_3 and 2-propanol-d_0 (blue bars in Figure S4b) is a clear indication that a fraction of MF formed only contains 2 rather than 3 Ds. This is consistent with proposed mechanism for the hydrogenolysis of furfural involving ring activation.

Derivation of kinetic isotope effect and theoretical background

Analysis of kinetics of FUR HDO in using deuterated solvent versus undeuterated solvent provides insight regarding mechanistic pathways and rate determining steps can be examined quantitatively. Because a deuterium atom has exactly twice the mass of a hydrogen atom, C-D and C-H bonds vibrate with different frequencies according to the equation

$$\upsilon = \frac{1}{2\pi}\ \kappa\ \ \mu \qquad \text{(S1)}$$

where κ is a force constant and μ is the reduced mass given by $\frac{m_{\mathrm{C}}m_{\mathrm{H}}}{m_{\mathrm{C}}+m_{\mathrm{H}}}$ or $\frac{m_{\mathrm{C}}m_{\mathrm{D}}}{m_{\mathrm{C}}+m_{\mathrm{D}}}$. Because of differences in vibrational frequencies, the vibrations energies are also different according to the equation

$$E_n = \left(n + \frac{1}{2}\right) h\upsilon \qquad \text{(S2)}$$

where n is the energy level (n = 0, 1, 2, …) and h is Planck's constant (6.626 × 10^{-34} m^2 kg^{-1}). Finally, because of vibrational energy differences between C-D and C-H bonds, the kinetics of bond scission of either C-D or C-H bonds are different. Assuming only vibrational energies are different, the rate constants for a given reaction are given by

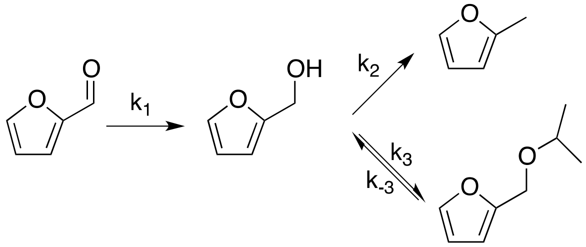
$$k_H = A_H e^{-\frac{E_{a,H}}{kT}} \qquad \text{(S3)}$$

$$k_D = A_D e^{-\frac{E_{a,D}}{kT}} \qquad \text{(S4)}$$

and by taking the ratio between the two,

$$\frac{k_H}{k_D} = \frac{A_H}{A_D} e^{-\frac{E_{a,H}-E_{a,D}}{kT}} = e^{\frac{h(\upsilon_H-\upsilon_D)}{2kT}} \qquad \text{(S5)}$$

where the ratio of rate constants is the kinetic isotope effect (KIE).



Scheme S5. Reaction pathway starting from FUR to FA and subsequently to 2-MF and 2-(isopropoxy)methylfuran (ether).

A system of ODEs described the chemical kinetics with simple power law expressions (equations S6-S9). The rate constants were approximated using nonlinear least-squares method via MATLAB's lsqnonlin function, yielding a model that fits the data very well (Figure S5). All rate equations were derived assuming irreversible reactions, except for the etherification reaction between FA and (isopropoxy)methylfuran, which we have previously shown is reversible[5]. The model reflects reversibility by incorporating an equilibrium constant, K_3.

$$r_{\mathrm{FUR}} = -k_1[\mathrm{FUR}][\mathrm{IPA}] \tag{S6}$$

$$r_{\mathrm{FA}} = k_1[\mathrm{FUR}][\mathrm{IPA}] - (k_2 + k_3)[\mathrm{FA}][\mathrm{IPA}] + \frac{k_3}{K_3}[\mathrm{E}] \tag{S7}$$

$$r_{\mathrm{E}} = k_3\left([\mathrm{FA}][\mathrm{IPA}] - \frac{1}{K_3}[\mathrm{E}]\right) \tag{S8}$$

$$r_{\mathrm{MF}} = k_2[\mathrm{FA}][\mathrm{IPA}] \tag{S9}$$

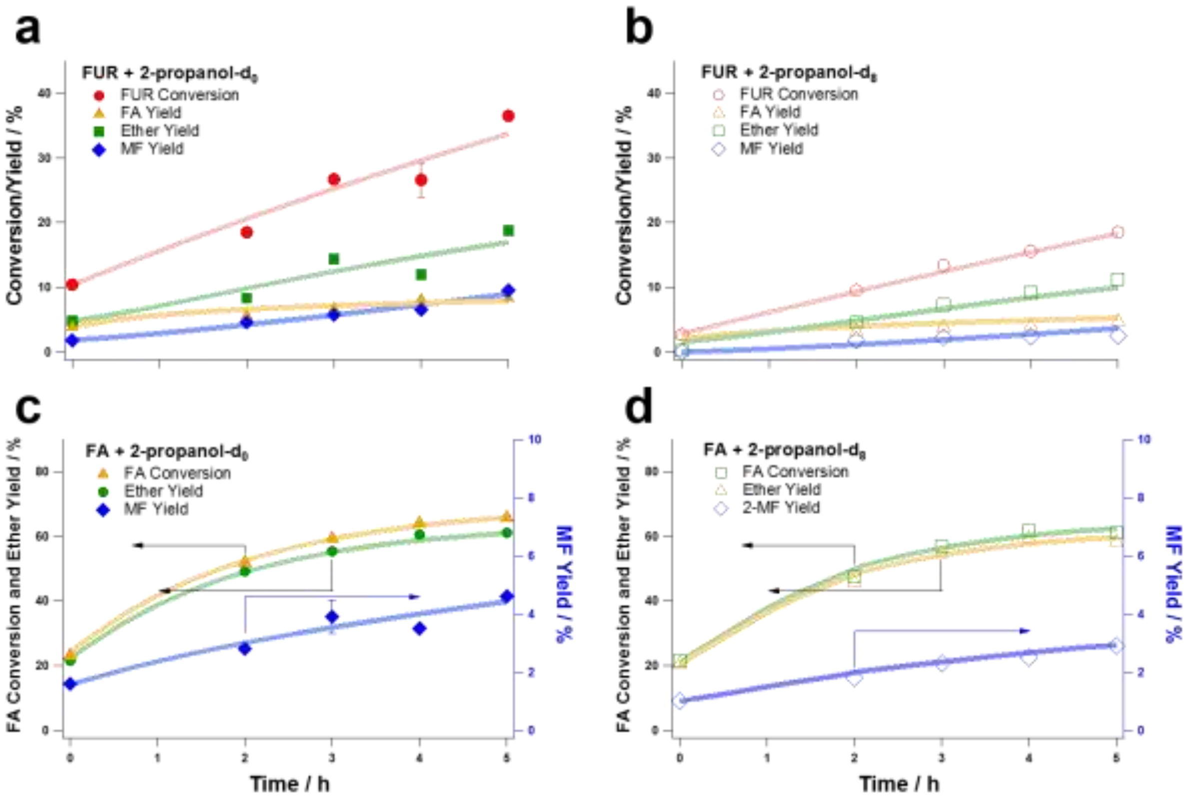


Figure S5. Kinetic data and all model fits for furfural HDO from 2-propanol-d_0 (A) and 2-propanol-d_8 (B) and for FA hydrogenolysis from 2-propanol-d_0 (C) and 2-propanol-d_8 (D).

References

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