Supplementary Materials

Kinetic and Mechanistic Study of Aldose Conversion to Functionalized Furans in Aqueous Solutions

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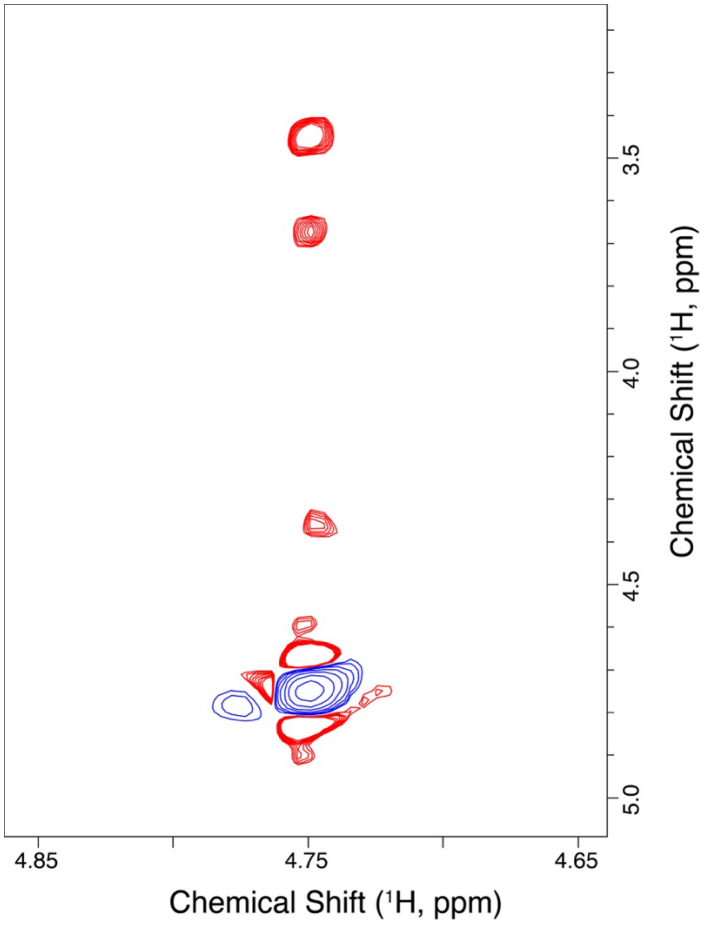

Figure S1. ^{1}H-^{1}H ROESY acquired rapidly on a reaction conducted with 0.05 equivalents triethylamine yields no crosspeak between H1 and H5 deriving from glucose in intermediate **2** due to the absence of pyran ring formation. Reaction conditions: 1 mmol aldose, 1.1 mmol malononitrile, 0.05 equivalents triethylamine, 288 K.

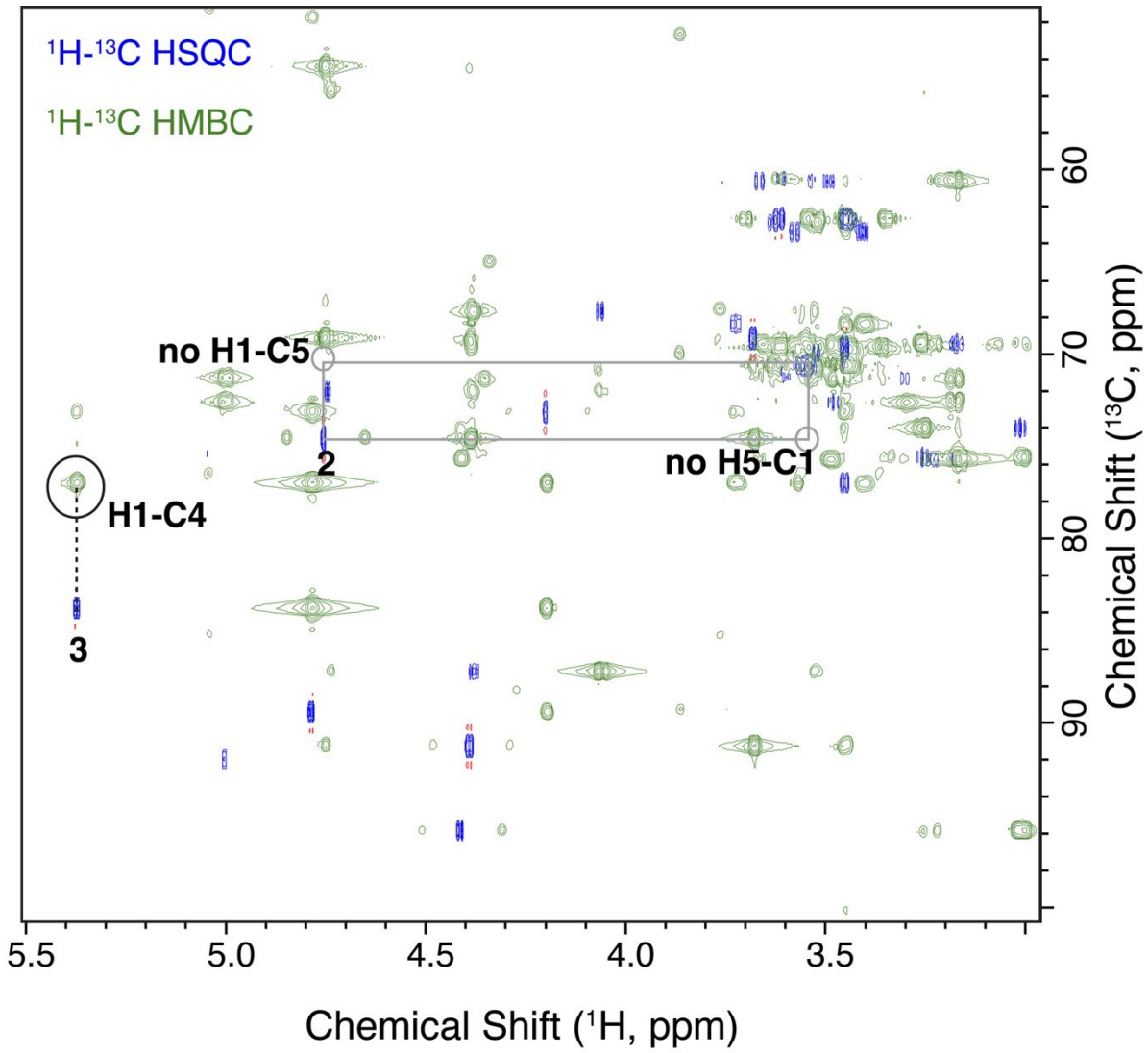

Figure S2. Overlay of ^{1}H-^{13}C HSQC (blue) and ^{1}H-^{13}C HMBC (green) acquired rapidly on a reaction conducted with 0.05 equivalents triethylamine yields no cross peak (grey lines) between H1 and C5 nor between H5 and C1 deriving from glucose in intermediate **2**, due to the absence of pyran ring formation. By contrast, H1 to C4 coupling in intermediate **2** positively identifies furanosyl-ring formation (black dashed line). Reaction conditions: 1 mmol aldose, 1.1 mmol malononitrile, 0.05 equivalents triethylamine, 288 K.

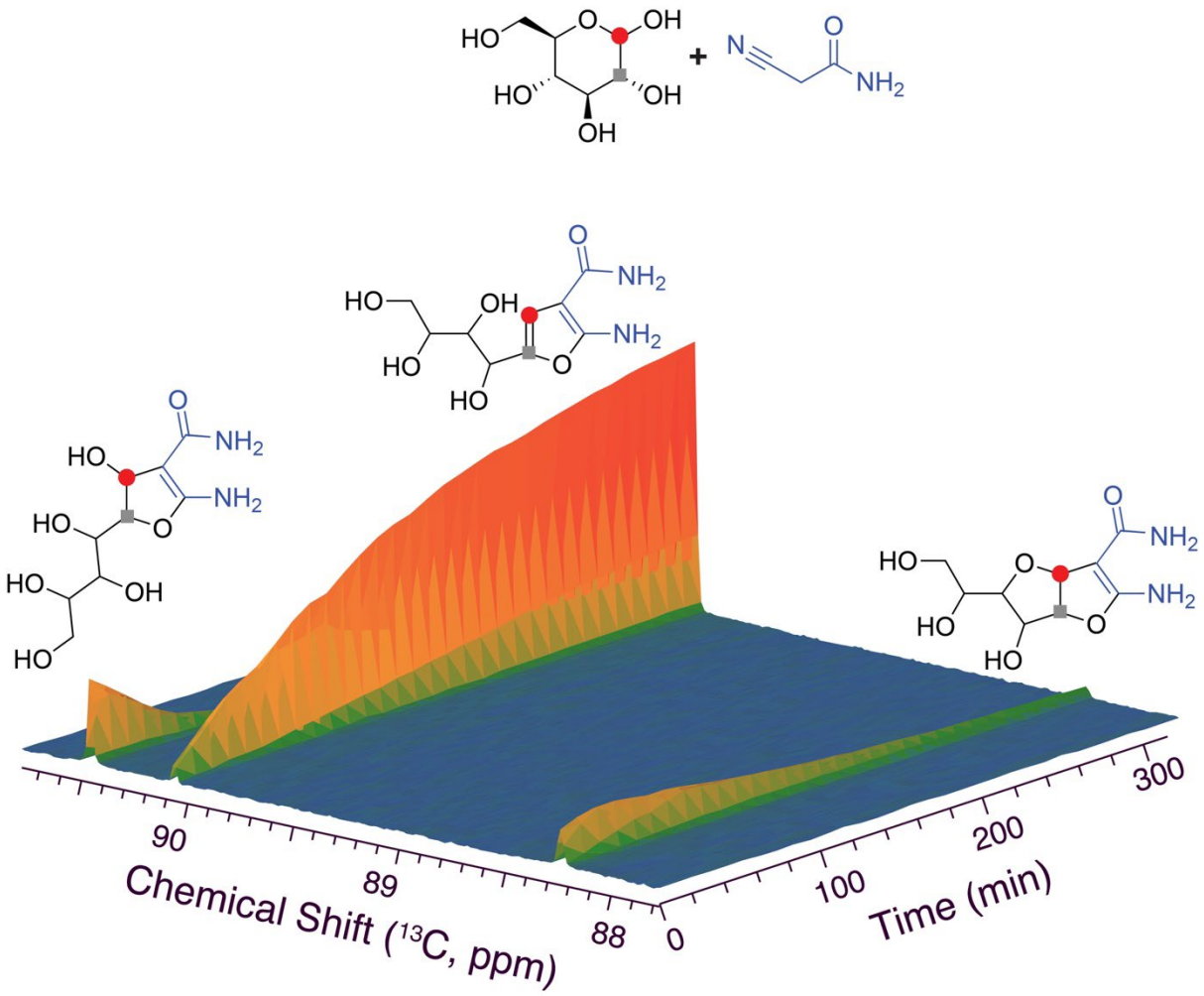

Figure S3. Time series of 1D ^{13}C NMR spectra in the conversion of glucose and cyanoacetamide. Positions deriving from C1 and C2 in glucose are schematically indicated in the observed intermediates and product. Reaction conditions: 1 mmol glucose (top) or 1.1 mmol cyanoacetamide (bottom), 0.25 mmol triethylamine, 313 K, 0.35 mL H_2O/0.05 mL D_2O.

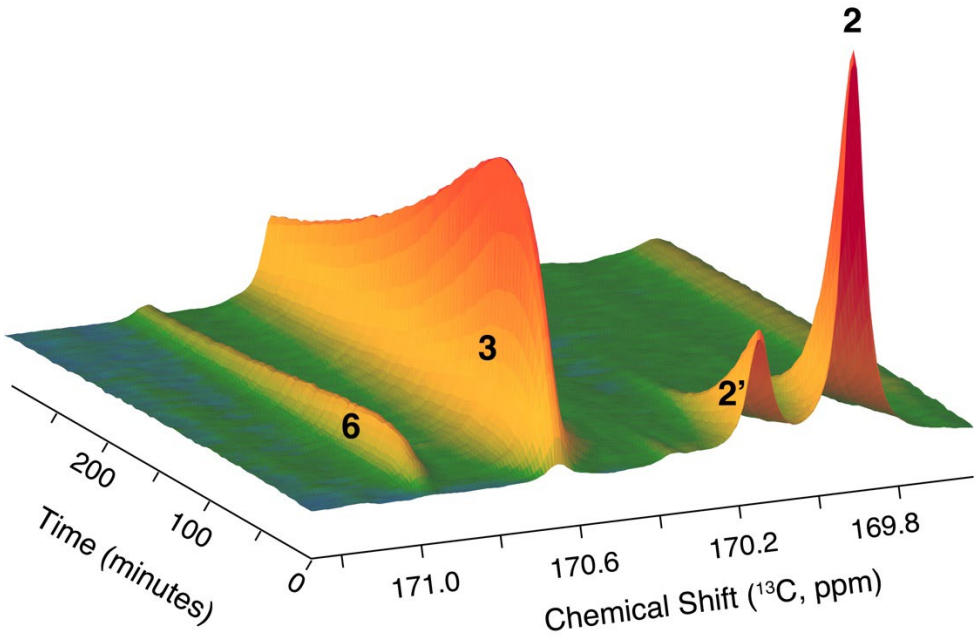

Figure S4. Minor forms formed in parallel to intermediates **2** (and its diastereomer **2′**) and **3** due to the formation of a stereogenic center at C1 upon Knoevenagel condensation to yield **2** and in the subsequent oxa-Michael addition by nucleophilic attack of $C4O4^-$ or $C5O5^-$ to the intermediate formed by completed Knoevenagel condensation to yield **3** and **6**, respectively.

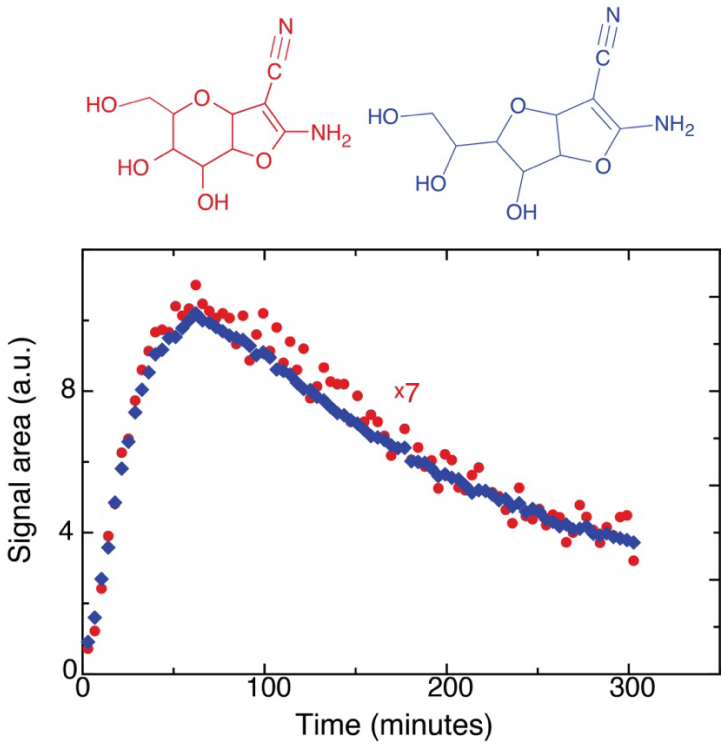

Figure S5. Kinetic profiles of signal areas for the bicyclic intermediates show similar kinetic profiles consistent with competing formation and conversion, plausibly due to equilibration that is rapid relative to product formation. The signal area for the minor bicyclic intermediate carrying a six-membered ring (red) is scaled by a 7-fold increase.

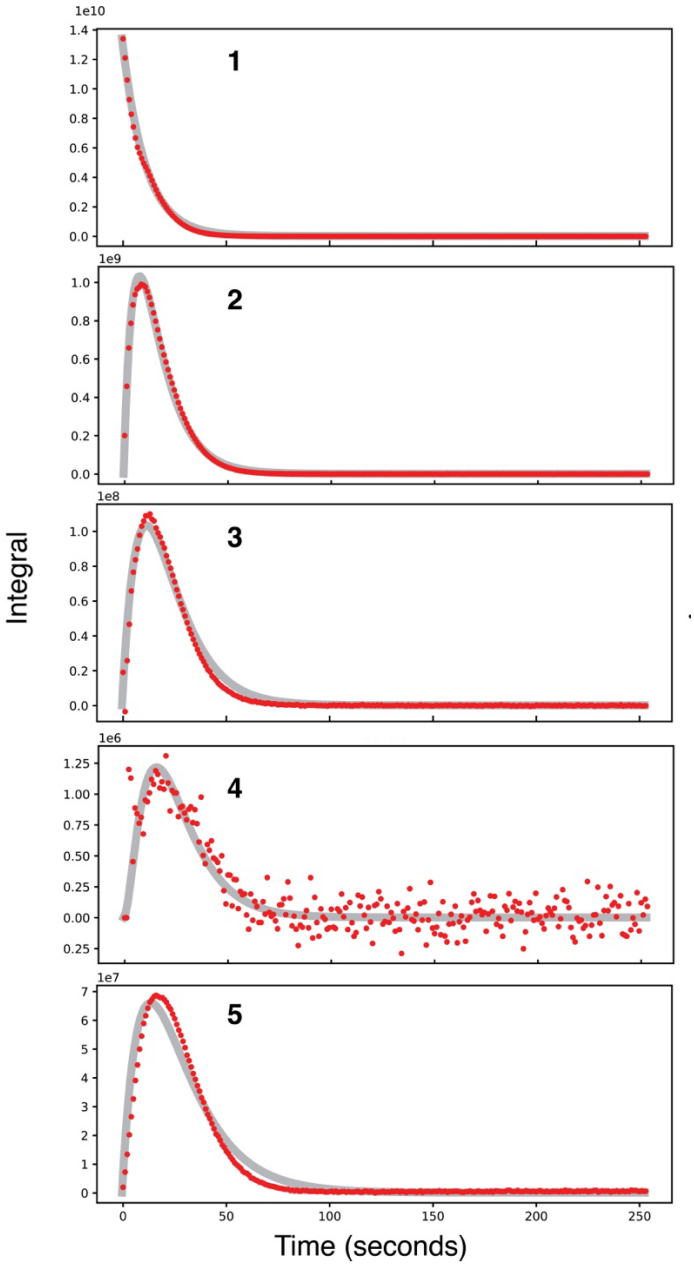

Figure S6. Fit of dDNP data to a kinetic model assuming the competitive formation of **2**, **3** and **5** from a transient population of intermediates as suggested in Scheme 2. dDNP data and conditions from Figure 5.

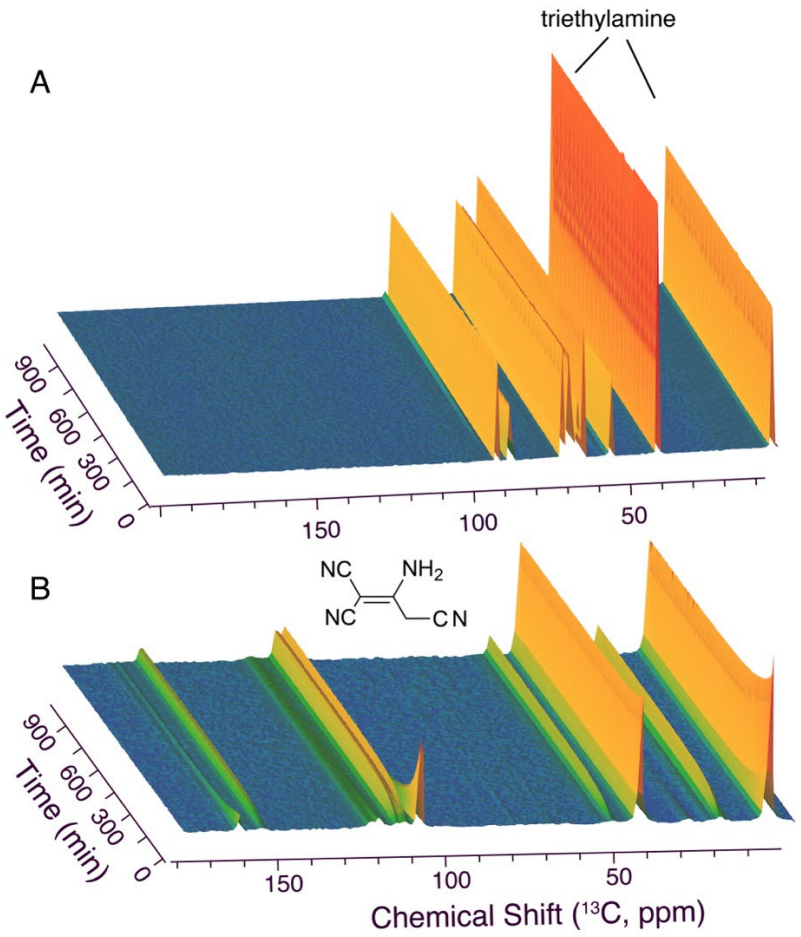

Figure S7. Stability of the individual reactants (top: glucose; bottom: malononitrile) under reaction conditions, indicating that the Knoevenagel reaction competes with dimerization of malononitrile (100% conversion within 15 hours), while aldose to ketose isomerization of glucose is less critical (9% conversion within 15 hours). Reaction conditions: 1 mmol glucose (top) or 1.1 mmol malononitrile (bottom), 0.15 mmol triethylamine, 298 K, 0.35 mL H_2O/0.05 mL D_2O.