

Supporting Information

Base-Catalyzed Cascades of Monosaccharide Conversion to Formic Acid: Isotope Tracking Reveals Pathways and Their Optimal Usage under Mild Conditions in Water

Stefan S. Warthegau,[#] Mette-Maya Siewertsen,[#] Robert Madsen, Sebastian Meier

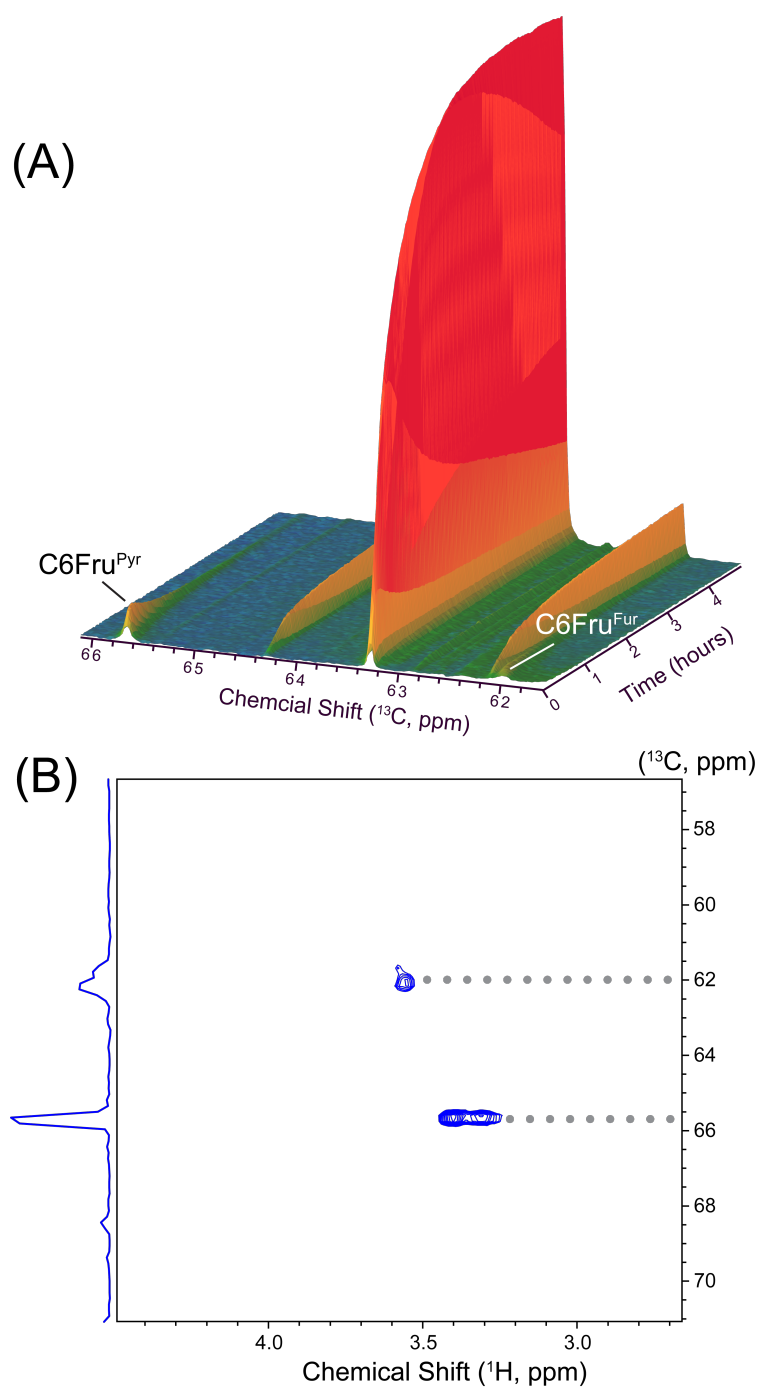


Figure S1: (Top) Time series of 1D ^{13}C NMR spectra for the ongoing conversion of [6- ^{13}C]glucose in the presence of lithium hydroxide and H_2O_2 showing the peak broadening of fructose C6 signals near 65.7 ppm and 62 ppm throughout the reaction progress. (Bottom) Spectral region of primary alcohol groups (C1 and C6 in fructose) in a ^1H - ^{13}C HSQC reference spectrum of fructose in the presence of 0.6 M LiOH. Only the fructose C6 signals near 65.7 ppm and 62 ppm in the ^{13}C dimension are detected, while the absence of distinct C1 signals indicates stronger broadening of the signal for the C1 position.

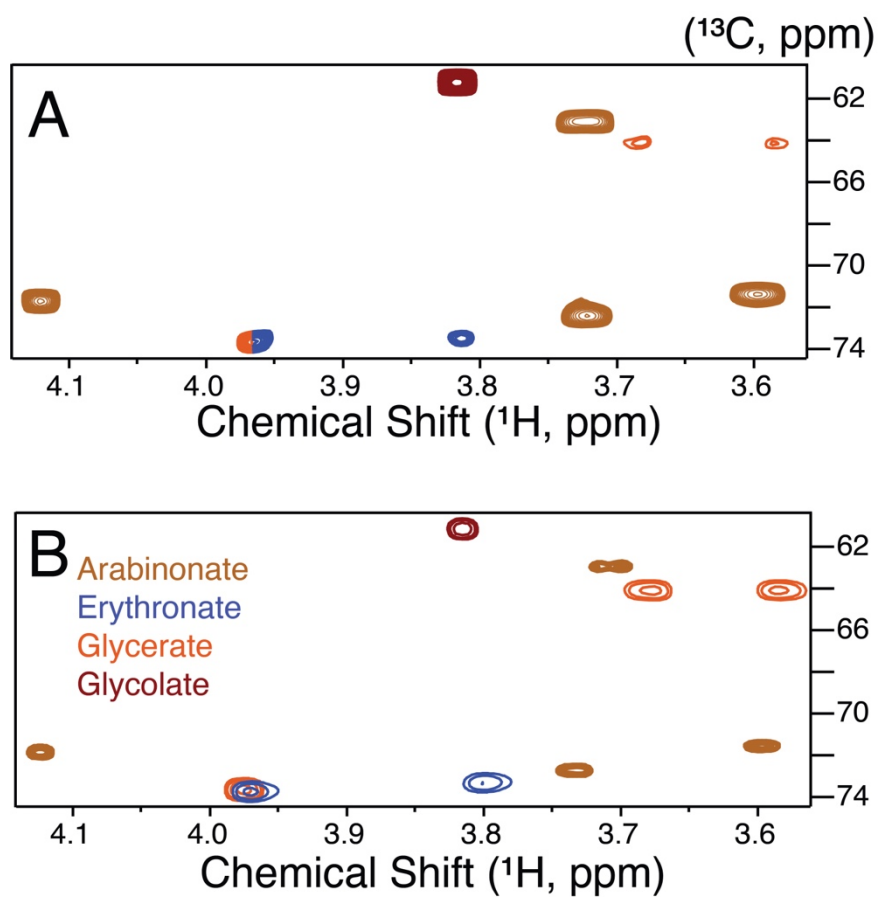


Figure S2. (A) ^1H - ^{13}C HSQC spectra for a product mixture after the conversion of 0.1 M glucose with 0.6 M lithium hydroxide and 6 equiv. hydrogen peroxide at 35 °C, 24 h. (B) Overlays of ^1H - ^{13}C HSQC spectra for authentic C2-C5 aldonic acids. Minor discrepancies in chemical shift can be ascribed to differences in pH.

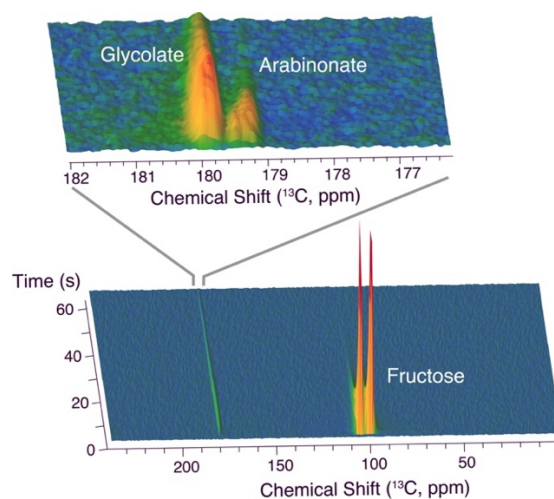


Figure S3. Time series of 1D ^{13}C NMR spectra for the conversion of hyperpolarized $[2\text{-}^{13}\text{C}]$ fructose in the presence of lithium hydroxide and hydrogen peroxide. Overall signal fades due to the temporary enhancement of signal via hyperpolarization and its loss with the T_1 time. Reaction conditions: 15 mM hyperpolarized $[2\text{-}^{13}\text{C}]$ fructose injected at $t=0$ s into 0.6 M LiOH and 6 equiv. hydrogen peroxide (after dissolution) in a 5 mm Shigemi NMR tube at 35 °C (11.4 T magnet).

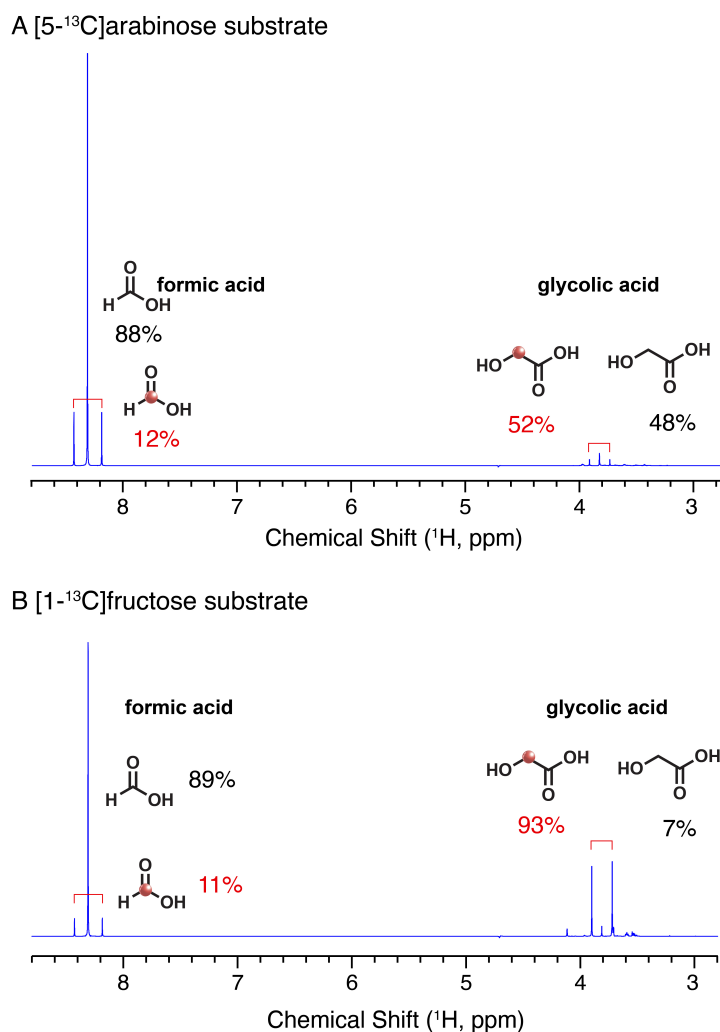


Figure S4. Representative quantitative ¹H NMR spectra acquired for product mixtures formed from 0.1 isotope labeled substrates after conversion with 0.6 M lithium hydroxide and 6 equiv. hydrogen peroxide at 35 °C, 24 h. Relative distributions between ¹³C and ¹²C containing CH groups in formate and glycolate are shown. (A) Spectra obtained for [5-¹³C]arabinose as the substrate show that significant amounts of glycolate and especially formate derive from unlabeled carbons, towards the reducing end. (B) Spectra obtained for [1-¹³C]fructose as the substrate show that glycolate is predominantly labeled and derives from cleavage near the keto group in the substrate, while the resultant tetrose from this cleavage predominantly converts to unlabeled formate.

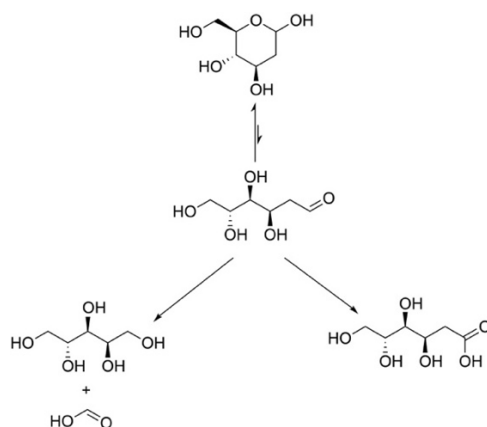


Figure S5. Products formed from 2-deoxyglucose (0.1 M) with 0.6 M lithium hydroxide and 6 equiv. hydrogen peroxide (6 equiv.) at 35 °C. Opposite to glucose, 2-deoxyglucose forms significant amounts of C6 aldonic acid, indicating that the 2-hydroxy group – if present – contributes to the C-C cleavage in carbohydrates (see Scheme S1). Nevertheless, conversion to formic acid and arabitol occurs in 2-deoxyglucose under the standard reaction conditions, corroborating the proposed C-C cleavage adjacent to carbonyls, resulting in replacement of the C-C bond with a hydroxy group on both carbons.

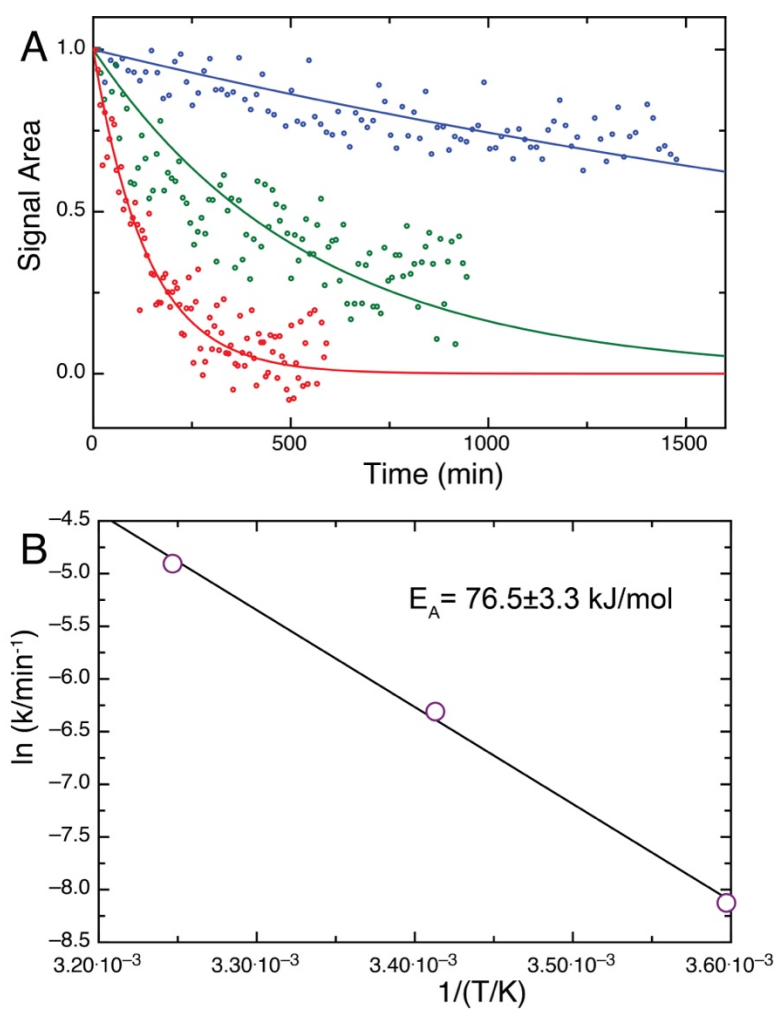
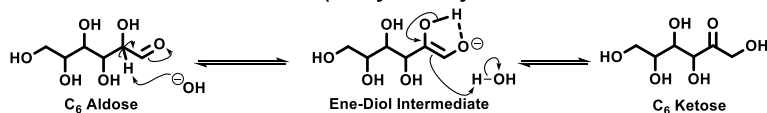
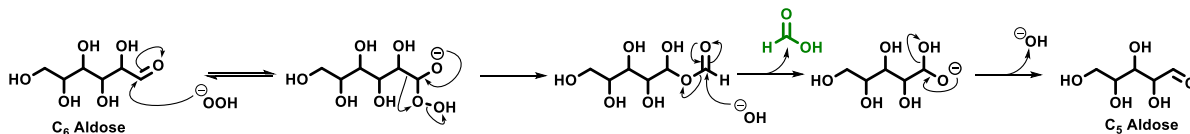


Figure S6. (A) Conversions at 278 K, 293 K and 308 K as tracked by time series of 1D ^{13}C spectra. (B) Arrhenius plot for the conversion of 0.1 M carbohydrate, 0.6 M lithium hydroxide with 6 equiv. hydrogen peroxide in 3 mm NMR sample tubes.

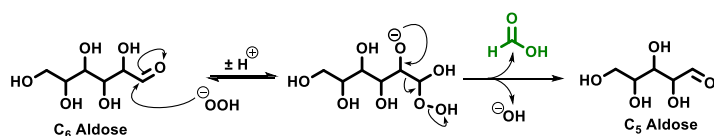
Aldose to Ketose Isomerization (Lobry de Bruyn-Van Ekelstein Transformation)



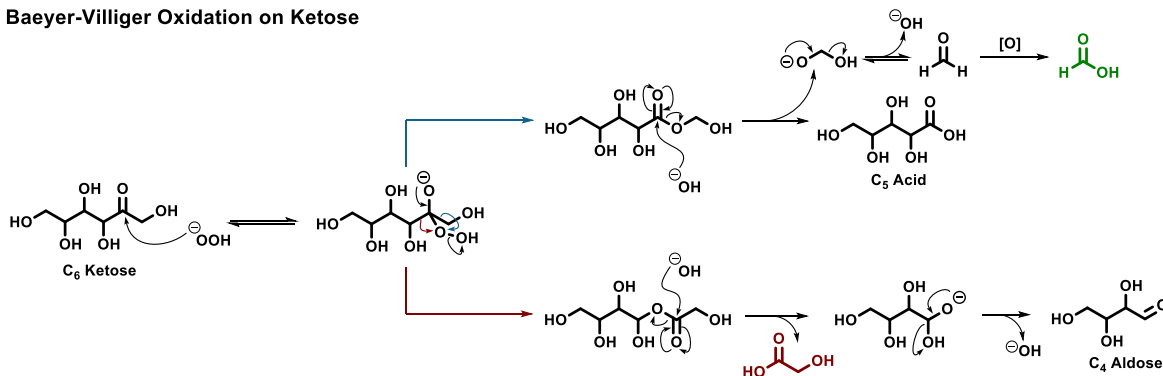
Baeyer-Villiger Oxidation on Aldose



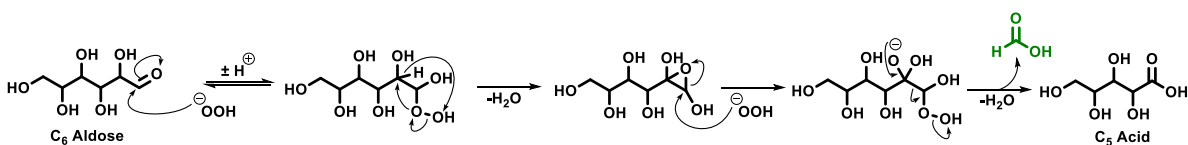
Oxidative C-C-cleavage of Aldose



Baeyer-Villiger Oxidation on Ketose



Proposed Formation of C₅ Acid from C₆ Aldose through Epoxidation



Scheme S1. Proposed arrow-mechanisms for the competing transformation of products in Scheme 2 and Scheme 3.

Table S1. Distribution of organic carbon in the reaction products formate and C2-C5 aldonates, depending on the substrate. Carbon fractions (%) for the different products are given.

Substrate		<i>Glucose</i>	<i>Mannose</i>	<i>Galactose</i>	
	Formate	73,4	93,2	94,3	
	Glycolate	4,3	2,3	2,2	
	Glycerate	1,6	0,7	0,8	
	C4 aldonate	0,8	2,0	1,5	
	C5 aldonate	19,9	1,8	1,2	
Substrate		<i>Arabinose</i>	<i>Lyxose</i>	<i>Ribose</i>	<i>Xylose</i>
	Formate	97,4	97,1	97,6	92,1
	Glycolate	1,2	1,2	1,1	1,7
	Glycerate	0,7	1,2	0,8	2,0
	C4 aldonate	0,7	0,5	0,5	4,2