Electronic Supplementary Information

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Experimental

1-, 2-, 3-, 4-, 5-, 6- and U-^{13}C-□-fructose (99%, Cambridge Isotope Laboratories), □-(-)-fructose (≥99.9%, Sigma), α-□-fructofuranose β-□-fructofuranose 1,2':2,3'-dianhydride (≥97.0%, Wako), d_6-dimethylsulfoxide (DMSO-d_6, >99.5+ atom % D, Sigma Aldrich), deuterium oxide (>99.8 atom D %, Armar), sodium bicarbonate (99.5%, Sigma-Aldrich), dichloromethane (RCI Labscan) and methanol (RCI Labscan, 99.9%), were all used as received.

NMR spectra were collected using a Bruker AV III 400 at ambient temperature. All one-dimensional ^{1}H and ^{13}C spectra were carried out with 30° flip angles. Quantitative ^{13}C peak areas were obtained for the singly-labeled samples using inverse-gated decoupling with recycle delays of 35 s for 1-^{13}C-□-fructose and 65 s for 2-^{13}C-□-fructose. Referencing was carried out with respect to 2.50 ppm for residual DMSO-d_5 for ^{1}H NMR, and 39.51 ppm for ^{13}C for DMSO-d_6. Chemical shifts are reported as ±0.005 ppm for ^{1}H and ±0.05 ppm for ^{13}C, but they generally shifted to ca. 0.1 ppm higher as a consequence of increasing water concentration with increasing carbohydrate conversion. The chemical shifts of intermediates are reported at the earliest conversion levels that they are observed at. J values were measured either from conventional 1D spectra or two-dimensional experiments, with spin simulation used to clarify small couplings (<2 Hz) and no attempt made to distinguish the sign of any of the scalar couplings. T_1 values were measured using the inversion recovery technique, and two-dimensional ^{1}H,^{1}H-DQF-COSY, ^{1}H,^{13}C-HSQC, HSQC-TOCSY (mixing time 0.15 s), HMBC and ^{1}H-decoupled ^{13}C,^{13}C-COSY experiments were used to assign peaks and connectivities, and measure some scalar couplings. For quantitative measurements, baselines were corrected and integrals adjusted for bias and slope where appropriate. For quantitative ^{1}H experiments, yields were calculated using an internal standard such as biphenyl (99.5%, Sigma-Aldrich), but in certain situations it was more convenient to use the solvent itself, residual DMSO-d_5 (T_1 ~10.3 s), or another internal standard such as methylsulfonyl methane (98%, Aldrich).

Most experiments were carried out with 65 mg fructose (0.36 mmol) and 0.5 mL solvent. The experiments in DMSO varying the H_2SO_4 concentration were performed by adding 0.1 mL of stock solutions of H_2SO_4 in DMSO to 0.31 mmol fructose dissolved in 0.4 mL DMSO-d_6, and the mixture heated at 120 °C for 2 h.

For the deuterium labeling experiments, the fructose hydroxyl protons were replaced with deuterium by repeated dissolution in D_2O and evaporation under reduced pressure, or, varying amounts of D_2O were added to the DMSO-d_6 fructose solution.

Between NMR experiments or repeated heating cycles in an oil bath, samples were stored at 4 °C unless otherwise specified. Isomerisation is relatively slow at room temperature, so that if a sample is heated to 150 °C then cooled, immediate measurements made at room temperature are representative of the sample at 150 °C.

Electronic Supplementary Information - Figures

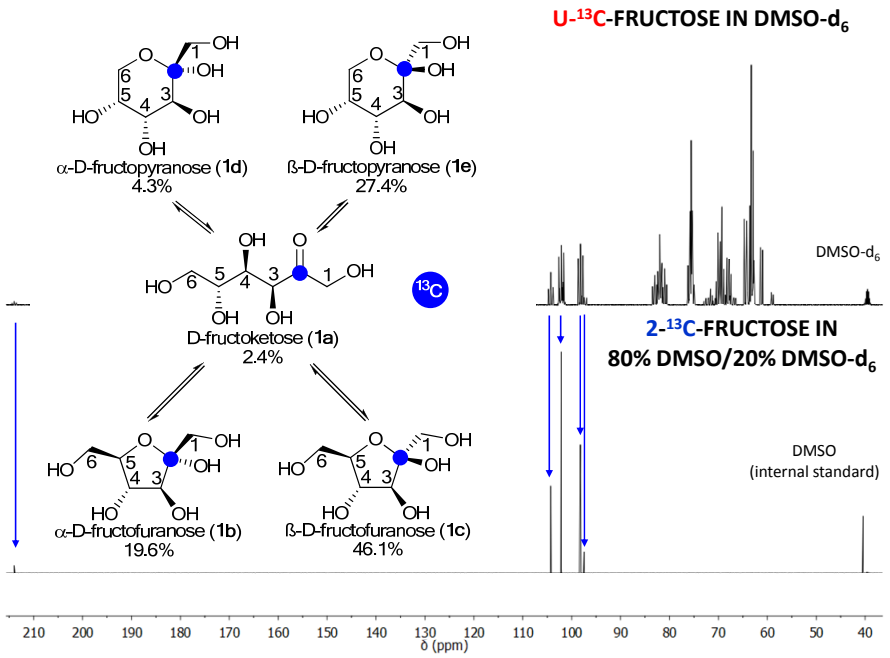


Fig S1. ^{13}C NMR of 0.36 mmol U-^{13}C-fructose in 0.5 mL DMSO-d_6 after dissolution (upper spectrum, a) and 0.36 mmol 2-^{13}C-fructose in 0.5 mL DMSO-d_6 at equilibrium at room temperature after one week (lower spectrum, b).

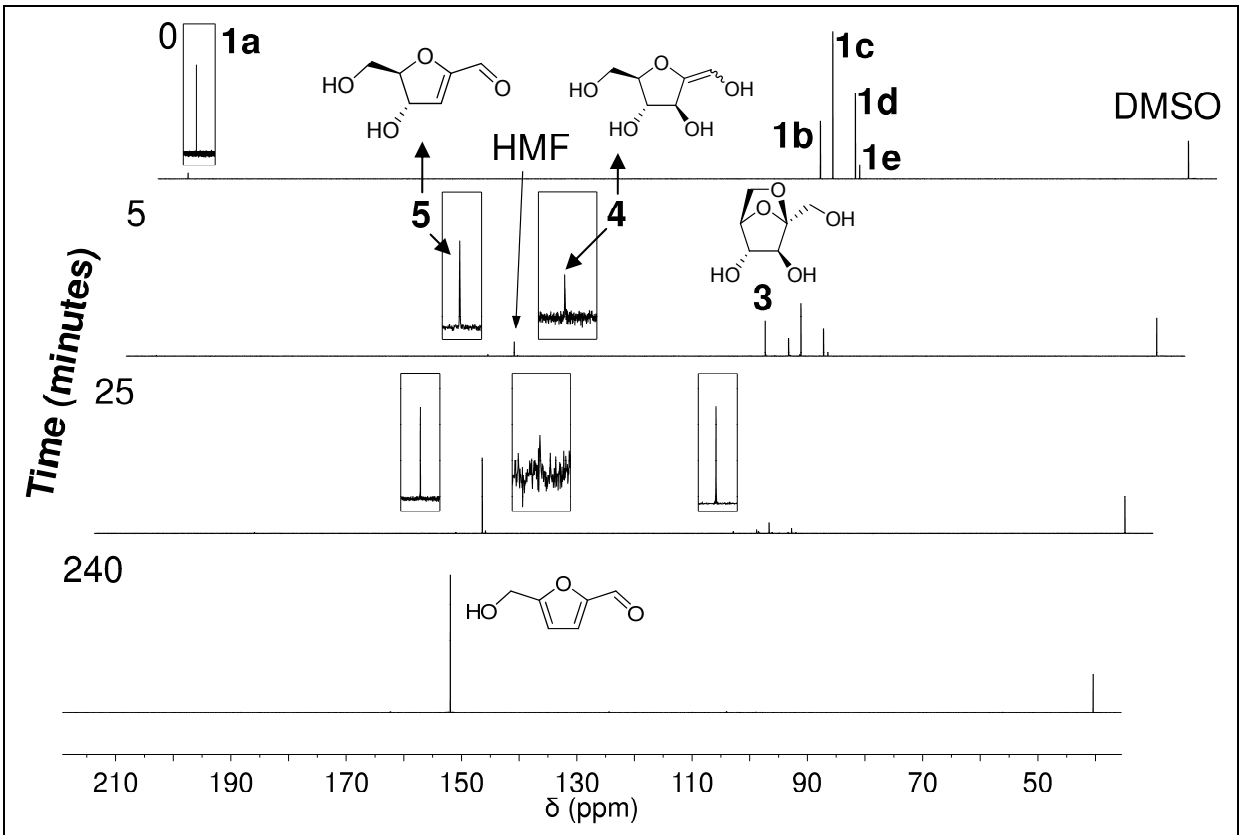


Fig S2. ^{13}C NMR of 0.36 mmol 2-^{13}C-fructose in 0.5 mL DMSO-d_6 at equilibrium at room temperature (top spectrum) and after heating at 150 °C for 5, 25, and 240 minutes.

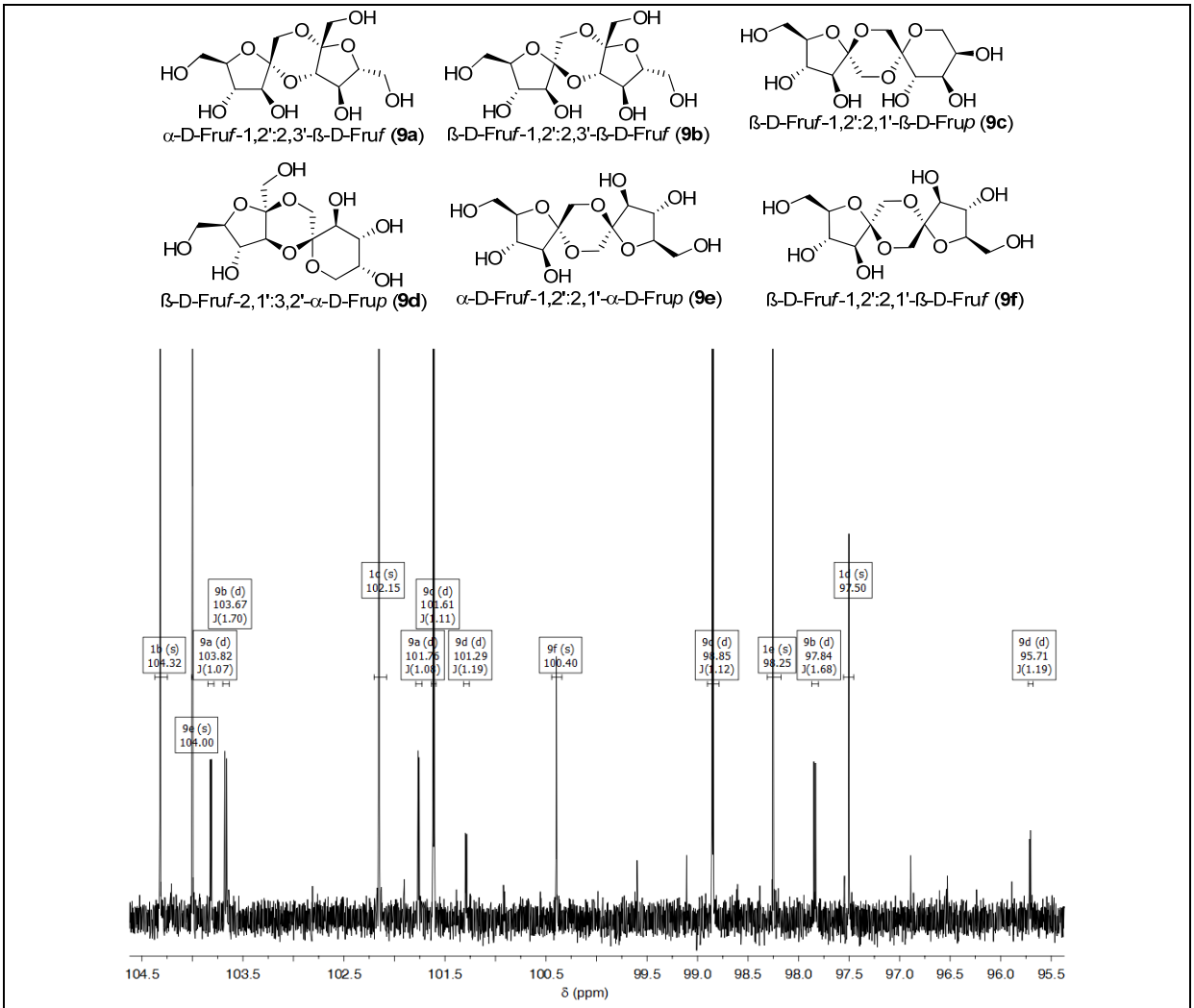


Fig S3. 2-^{13}C-fructose in DMSO-d_6, after heating at 150 °C for 25 min. The assignment of **9a** is confirmed by comparison with in an authentic standard. **9b-f** were assigned by comparison with literature data in D_2O[1] with **9e** and **9f** also being the only two detectable symmetric DFAs. Abbreviations: **9a**, α-□-fructofuranose ß-□-fructofuranose 1,2':2,3'-dianhydride; **9b**, ß-□-fructofuranose ß-□-fructofuranose 1,2':2,3'-dianhydride; **9c**, ß-□-fructofuranose ß-□-fructopyranose 1,2':2,1'-dianhydride; **9d**, ß-□-fructofuranose α-□-fructopyranose 2,1':3,2'-dianhydride; **9e**, α-□-fructofuranose α-□-fructofuranose 1,2':2,1'-dianhydride; **9f**, ß-□-fructofuranose ß-□-fructofuranose 1,2':2,1'-dianhydride.

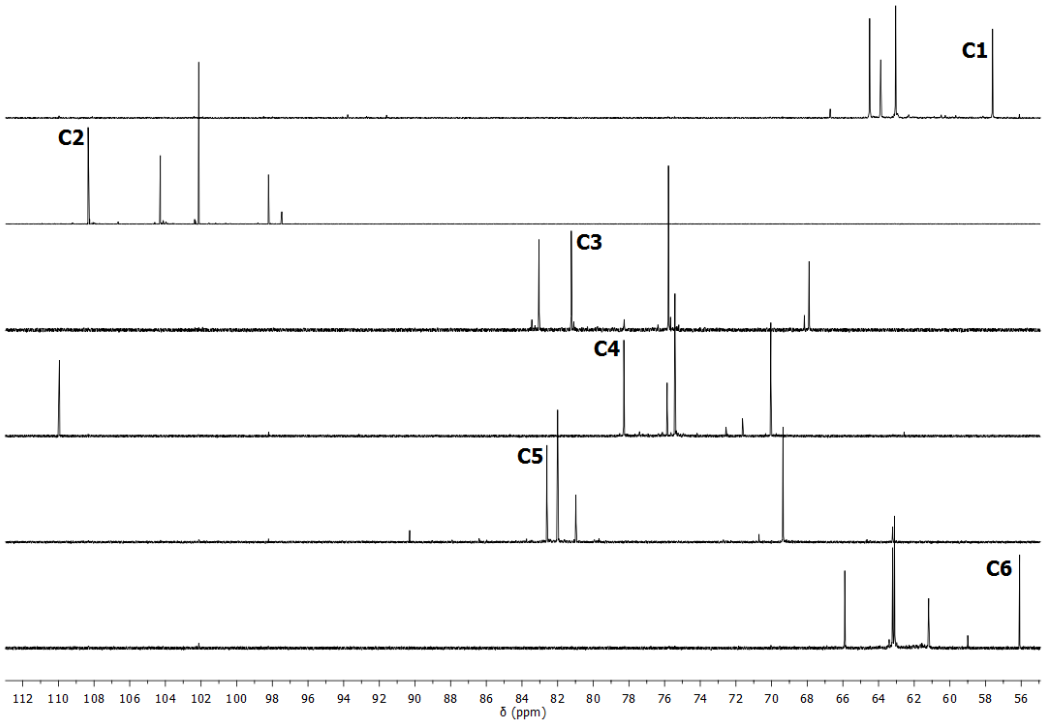


Fig S4. Typical ^{13}C NMR spectra of the reaction mixtures using singly-labelled 1-^{13}C- (top), 2-^{13}C, 3-^{13}C, 4-^{13}C, 5-^{13}C, or 6-^{13}C (bottom) fructoses, with assignments for 2,6-anhydro-β-□-fructofuranose (3).

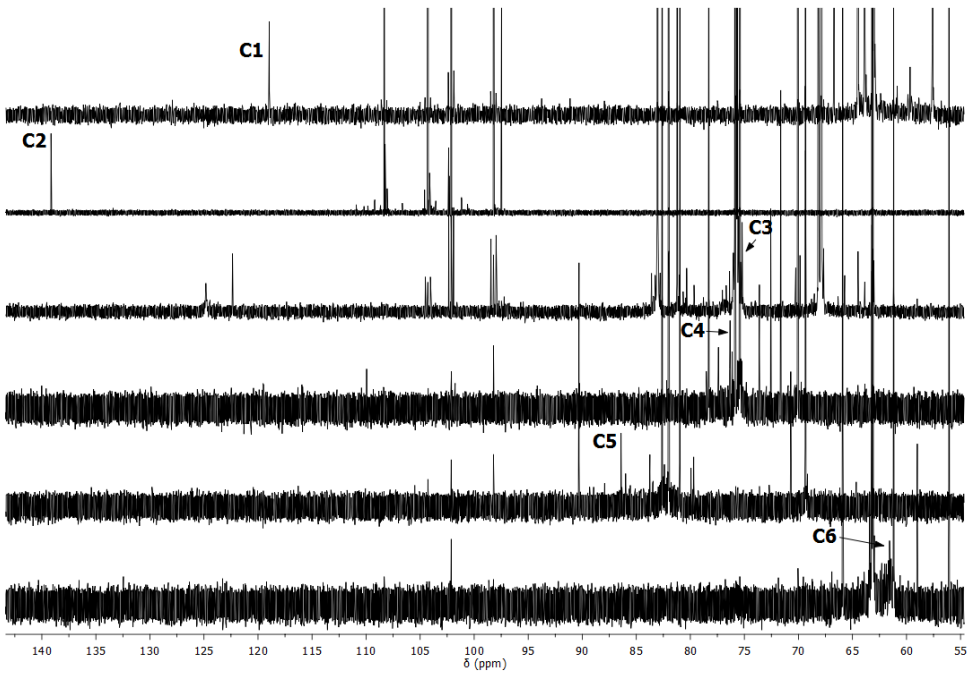


Fig S5. Typical ^{13}C NMR spectra of the reaction mixtures using singly-labelled 1-^{13}C- (top), 2-^{13}C-, 3-^{13}C-, 4-^{13}C- 5-^{13}C-, or 6-^{13}C- (bottom) fructoses, with assignments for (2*R*,3*S*,4*S*)-2-(hydroxymethyl)-5-(hydroxyl-methylene)-tetrahydrofuran-3,4-diol (4).

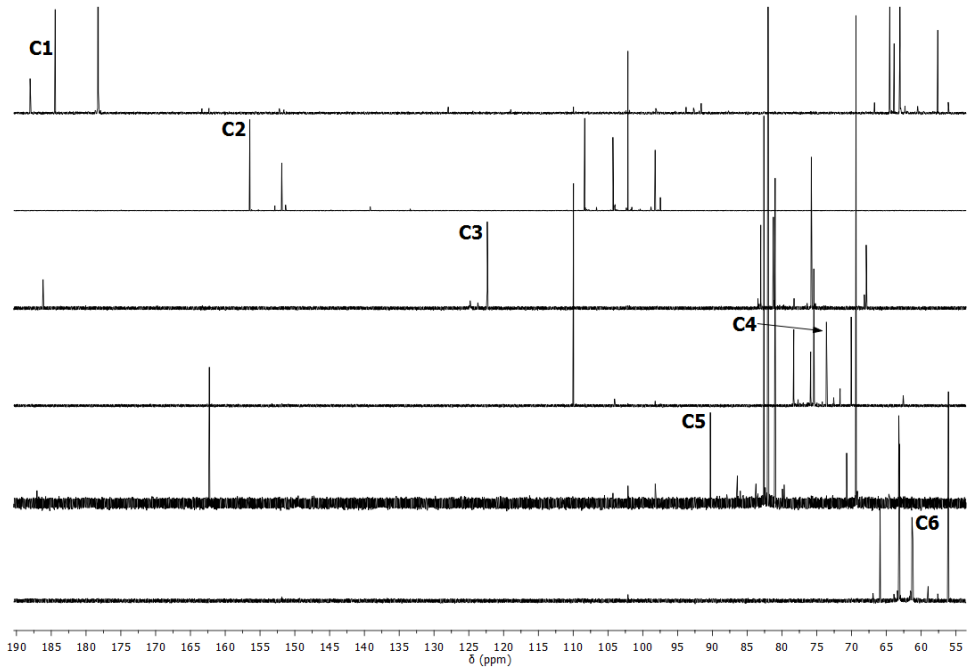


Fig S6. Typical ^{13}C NMR spectra of the reaction mixtures using singly-labelled 1-^{13}C- (top), 2-^{13}C-, 3-^{13}C-, 4-^{13}C-, 5-^{13}C-, or 6-^{13}C- (bottom) fructoses, with assignments for (4*S*,5*R*)-4-hydroxy-5-hydroxymethyl-4,5-dihydrofuran-2-carbaldehyde (5).

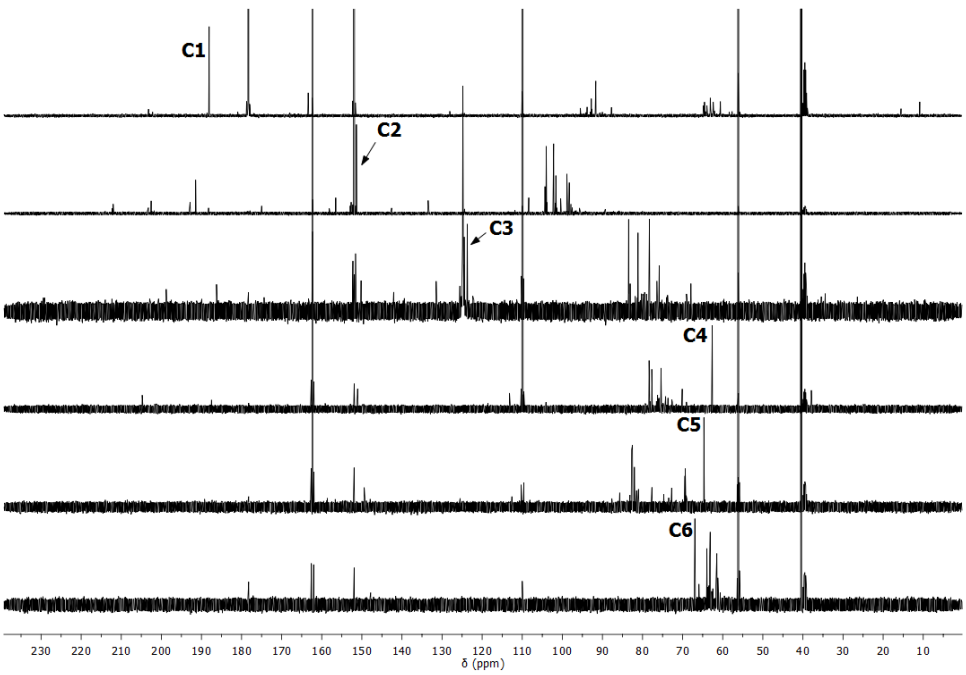


Fig S7. Typical ^{13}C NMR spectra of the reaction mixtures using singly-labelled 1-^{13}C- (top), 2-^{13}C-, 3-^{13}C-, 4-^{13}C-, 5-^{13}C-, or 6-^{13}C- (bottom) fructoses, with assignments for (3*R*,4*S*)-3,4-dihydroxy-3,4-dihydro-2H-pyran-6-carbaldehyde (8).

Electronic Supplementary Information – Tables

Table S1. NMR data for 2,6-anhydro-β-□-fructofuranose (**3**). The data are comparable to literature data in DMSO-d_6 and MeOD-d_4.[2, 3] [a] Measured using singly ^{13}C-labeled fructose reaction mixtures.

Position	δ_H (ppm)	J_{HH} (Hz)	δ_C (ppm)	J_{CC} (Hz)
1	3.59 (m)	-	57.6 (d)	51.7 (C-2)
2	-	-	108.3 (dd)	51.7 (C-1), 44.4 (C-3)
3	3.68 (dt)	3.9 (H-4), 1.4 (H-1' and H-4)	81.2 (dd)	44.5 (C-2), 40.4 (C-4), 4.0 (C-1)[b]
4	3.51 (d)	1.1 (H-3)	78.3 (dd)	39.7 (C-3), 38.9 (C-5), 1.5 (C-1)[a]
5	4.38 (dd)	4.0 (H-6'), 1.5 (H-4)	82.6	2.8 (C-1)[a], 1.7 (C-2)[a]
6	3.53 (d)	7.1 (H-6')	65.9 (d)	33.8 (C-5)
6'	3.41 (dd)	6.9 (H-6), 4.2 (H-5)		

Table S2. NMR data for 5-(hydroxymethyl)-2-furaldehyde (HMF). [a] Measured using singly ^{13}C-labelled HMF where possible.

Position	δ_H (ppm)	J (Hz)	δ_C (ppm)	J_{HH} (Hz)[a]
1	9.52 (s)	-	177.9 (dt)	67.7 (C-2), 9.2 (C-3), ~3.4 (C-4), 3.0 (C-5)
2	-	-	151.6 (tdd)	67.6 (C-1), 66.5 (C-3), 4.3 (C-5), 2.5 (C-6)
3	7.48 (d)	3.5 (H-4)	124.5 (br. t)	67.6 (C-4), ~56.6 (C-2)
4	6.59 (dt)	3.5 (H-3), 0.7 (H-6)	109.9 (dddd)	67.2 (C-5), 50.1 (C-3), 6.1 (C-6), 3.5 (C-1)
5	-	-	162.0 (dddd)	67.1 (C-4), 57.1 (C-6), 4.2 (C-2), 2.8
6	4.49 (s)	-	56.0 (ddt)	57.1 (C-5), 6.2 (C-4), 2.5 (C-3), 2.3 (C-2)

Table S3. NMR data for (2*R*,3*S*,4*S*)-2-(hydroxymethyl)-5-(hydroxymethylene)-tetrahydrofuran-3,4-diol (**4**). The data are similar to the peracetate, in particular, the *E* isomer, but an unequivocal assignment of the enol geometry of **4** is not possible.[1] [a] Tentative assignment.

Position	δ_H (ppm)	J_{HH} (Hz)	δ_C (ppm)	J_{HH} (Hz)
1	5.57 (d)	1.1 (H-3)	118.9 (dd)	96.7 (C-2), 8.3 (C-3)
2	-	-	139.1 (ddd)	96.7 (C-2), 52.2 (C-3), 3.9
3	4.11 (dd)	3.7 (H-4), 1.3 (H-1)	75.2	-
4	3.74	-	76.3[a]	-
5	3.83	-	86.4 (br. t)	39.9 (C-4 and C-6)
6	3.55	-	61.5 (d)	49.5 (C-5)
6'	3.44	-		

Table S4. NMR data for (4*S*,5*R*)-4-hydroxy-5-hydroxymethyl-4,5-dihydrofuran-2-carbaldehyde (**5**). Data are comparable to those for the methyl and benzyl ethers[4] and for *tert*-butyldimethylsilyl derivatives where C-1 is a ketone.[5] [a] Tentative assignment.

Position	δ_H (ppm)	J_{HH} (Hz)	δ_C (ppm)	J_{CC} (Hz)
1	9.47 (s)	-	184.3 (dddd)	60.7 (C-2), 9.5 (C-3), 4.2 (C-4), 2.3
2	-	-	156.4 (ddd)	72.8 (C-3), 60.7 (C-1), 2.4
3	6.25 (d)	2.9 (H-4)	122.3 (ddd)	73.1 (C-2), 43.1 (C-4), 9.4 (C-1)
4	4.81 (dd)	4.4 (H-5), 2.9 (H-3)	73.6 (dddd)	45.9 (C-3), 38.4 (C-5), 4.3 (C-1), 2.6 (C-6)
5	4.26 (td)	5.3 (H-6')[a], 4.4 (H-4)	90.3 (ddd)	41.8 (C-6), 38.4 (C-4), 1.7
6	3.46 (m)	-	61.3 (dd)	42.1 (C-5), 2.5 (C-4)

Table S5. Partial NMR data for (3*S*,4*R*,5*R*)-2-(hydroxymethylene)-tetrahydro-2*H*-pyran-3,4,5-triol (**7**). Data are similar to those for the corresponding peracetates.[6] Further characterization of C-3-C-6 using 2D techniques from 3-^{13}C-fructose was not possible due to the low concentration and overwhelmingly high concentration of other carbohydrates. [a] Tentative. [b] Calculated using Modgraph NMRPredict as part of MestReNova 6.0.2.

Position	δ_H (ppm)	J_{HH} (Hz)	δ_C (ppm)	J_{CC} (Hz)
1	6.61	-	127.9 (dd)	92.4 (C-2), 10.0 (C-3)
2	-	-	133.4 (ddd)	92.7 (C-1), 62.7 (C-3), 15.5
3	4.48	2.1 (H-4)	68.3	
4	3.81		71.2[b]	
5	3.23[a]		67.5[b]	
6	4.26[b]		68.1[b]	
6'	4.45[b]			

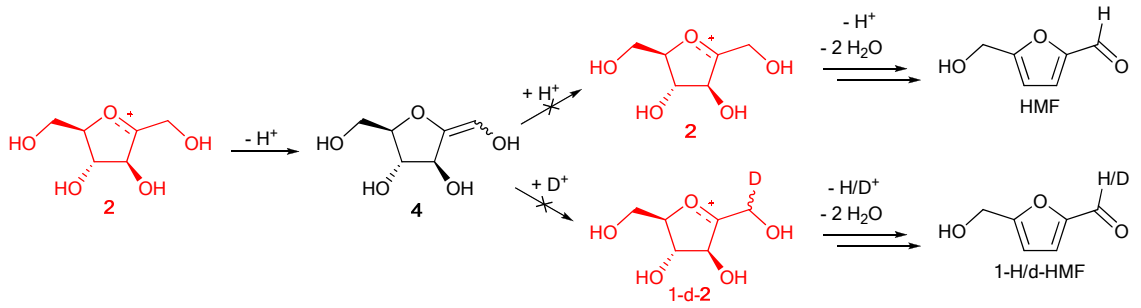
Table S6. Partial NMR data for (3*R*,4*S*)-3,4-dihydroxy-3,4-dihydro-2*H*-pyran-6-carbaldehyde (**8**). Data is comparable to those for the benzoyl ester.[7]

Position	δ_H (ppm)	J (Hz)	δ_C (ppm)	J_{CC} (Hz)
1	9.13 (s)	-	187.9 (dddd)	60.5 (C-2), 9.8 (C-3), 4.7, 2.3
2	-	-	151.3	-
3	5.88 (dd)	3.8 (H-4), 0.8 (H-1)	123.7	-
4	4.30 (td)	4.1 (H-3 and H-5), 1.3 (H-6)	62.6	-
5	3.75	-	64.7	-
6	3.89	-	66.9	-

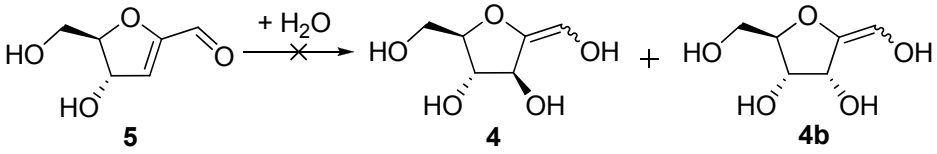
Table S7. NMR data for α-□-fructofuranose ß-□-fructofuranose 1,2':2,3'-dianhydride (**9a**). The unprimed numbers are for the α-furanose ring, and the primed numbers the β-furanose. [a] Measured using 2-^{13}C-fructose.

Position	**δ_H (ppm)**	**J_{HH} (Hz)**	**δ_C (ppm)**	**J_{CC} (Hz)[a]**
1a	3.77	12.4 (H-1b)	58.3	
1b	3.50	12.3 (H-1a)		
2	-	-	103.8	1.1 (C-2')
3	3.83	4.5 (H-4)	81.7	
4	3.57	5.1 (H-3)	76.2	
5	3.77	(m)	82.5	
6a	3.50	11.3 (H-6b), 4.4 (H-5)	61.2	
6b	3.36	11.8 (H-6a), 5.7 (H-5)		
1a'	3.38	11.5 (H-1b')	64.3	
1b'	3.30	11.5 (H-1a')		
2'	-	-	101.7	1.1 (C-2)
3'	4.16	6.7 (H-4')	78.9	
4'	4.33	6.9 (H-3' and H-5')	72.7	
5'	3.40	7.3 (H-4'), 5.6 (H-6a' or H-6b'	81.5	
6a'	3.61	(m)	61.0	
6b'	3.42	(m)		

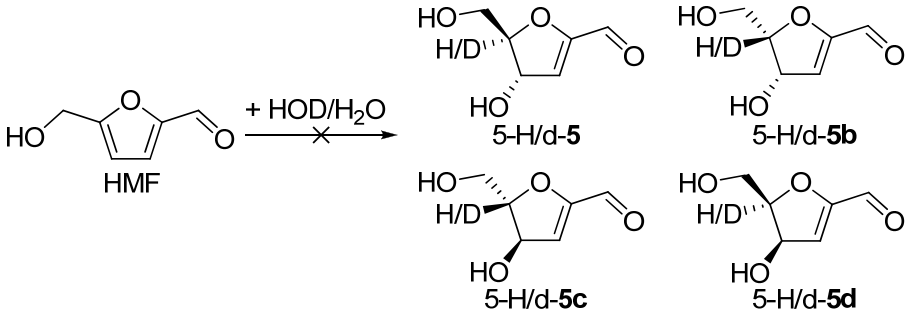
Electronic Supplementary Information – Schemes



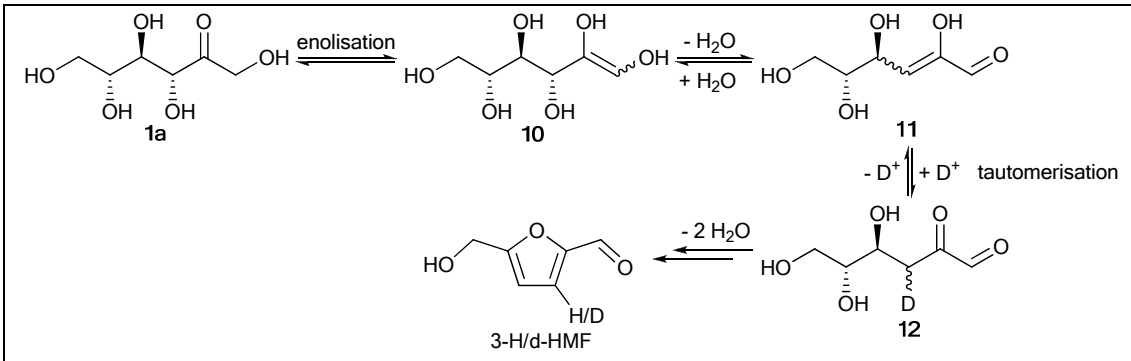
Scheme S1. The reversible deprotonation of **2** to **4** in the presence of exchangeable deuterium could lead to the formation of HMF and 1-d-HMF with deuterium at the aldehyde group. There was no evidence for the formation of 1-d-HMF.



Scheme S2. The addition of water to **5** could lead to the formation of (2*R*,3*S*,4*S*)-2-(hydroxymethyl)-5-(hydroxymethylene)tetrahydrofuran-3,4-diol (**4**) and (2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-(hydroxymethylene)tetrahydrofuran-3,4-diol (**4b**). Only the formation of **4** was observed.



Scheme S3. The addition of water to HMF in the presence of exchangeable deuterium could lead to the formation of a mixture of stereoisomers of **5**. Only the formation of (4*S*,5*R*)-4-hydroxy-5-hydroxymethyl-4,5-dihydrofuran-2-carbaldehyde (**5**) was observed.



Scheme S4. The role of the linear **1a** in the formation of HMF requires the intermediate formation of 1,2-enediol (**10**), and the dicarbonyl 3-deoxy-□-*erythro*-hexose-2-ulose (**12**).[8] Less than 1% deuterium was incorporated at C-3 of HMF, allowing us to rule out the importance of this pathway.

Electronic Supplementary Information – References

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