Electronic Supplementary Material (ESI) for ChemComm.

Furanosic forms of sugars: Conformational equilibrium of methyl β-D-ribofuranoside

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Supplementary Information

<u>Contents</u>:

Experimental

In FT-MW spectroscopy short microwave pulses transmitted into an evacuated Fabry-Perot resonator are used to induce a macroscopic polarization in molecules with a permanent electric dipole moment. The subsequent rotational coherence decay is digitally recorded in the time domain, averaged and Fourier transformed to the frequency domain to yield the resonance frequencies. The resonator is mechanically tuned to scan the desired spectral regions within the operating range of the instrument (6-18 GHz). The accuracy of the frequency measurements is better than 3 kHz. Rotational transitions separated less than 10 kHz are resolvable.

Methyl β-D-ribofuranoside was synthesized as follows.[1] Concentrated H_2SO_4 (0.3 mL) was added to a solution of D-ribose (5.0 g, 33 mmol) in anhydrous MeOH (50 mL) in an ice bath with stirring. The resulting solution was stirred for 16 h and neutralized by addition and stirring with an ion exchange resin (Amberlite IRA-400(OH)). The mixture was filtered, the resin washed with methanol (4 x 25 mL) and the solvent was removed from the filtrate under vacuum and then azeotroped with toluene to give crude methyl D-ribofuranoside as a yellow oil mixture of anomers (4:1 β:α, 4.3 g, 79% yield) which were separated by repeated flash chromatography (15% MeOH/EtOAc) to yield pure β anomer which was lyophilized from water: $[\alpha]_D^{20}$ (c, 1.3 MeOH) = - 55.4 {$[\alpha]_D^{20}$ (c, 1.0 MeOH) = -62.4}; ^{13}C NMR (D_2O) δ 107.2, 82.0, 73.5, 70.0, 62.1, 54.4. The sample was later prepared as a solid cylindrical rod by addition of a commercial binder and vaporized by laser ablation from a picosecond-pulsed Nd:YAG laser operating in the third harmonic (355 nm). The near simultaneous coexpansion with a Ne carrier gas (5-6 bar) through the 0.8 mm ablation nozzle created the supersonic jet.

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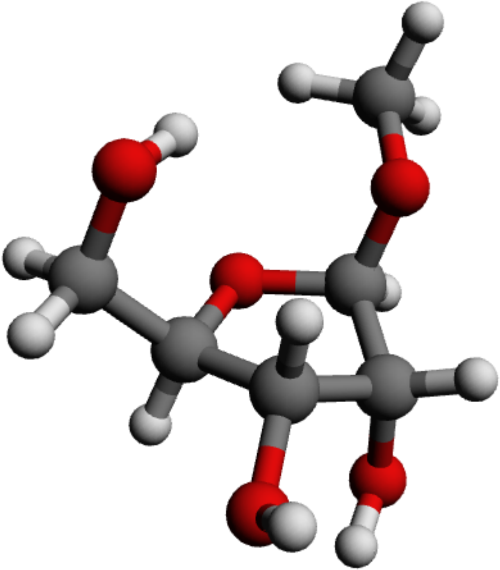
[1] Barker, G. R.; Smith, D. C. C.. *J. Chem. Soc.*, **1954**, 2151.

Figures S1 and S2 (pages 4 and 5). Interactive view (pdf only) of the MP2 structure of the two observed conformers.



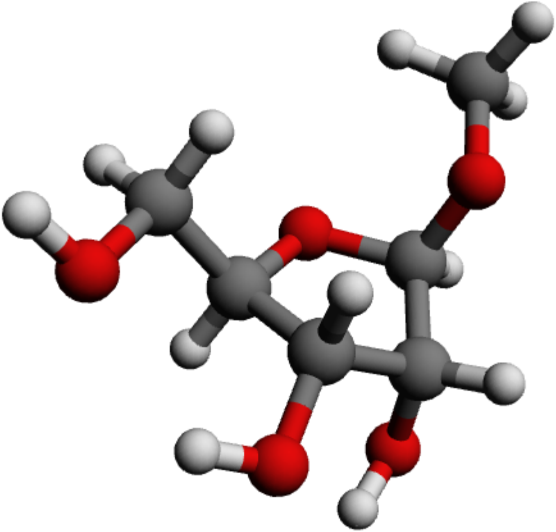


Figure S3. Experimental rotational spectrum of β-D-ribofuranoside and comparison to the simulated spectra of conformers 1 and 2 based on fitted parameters.

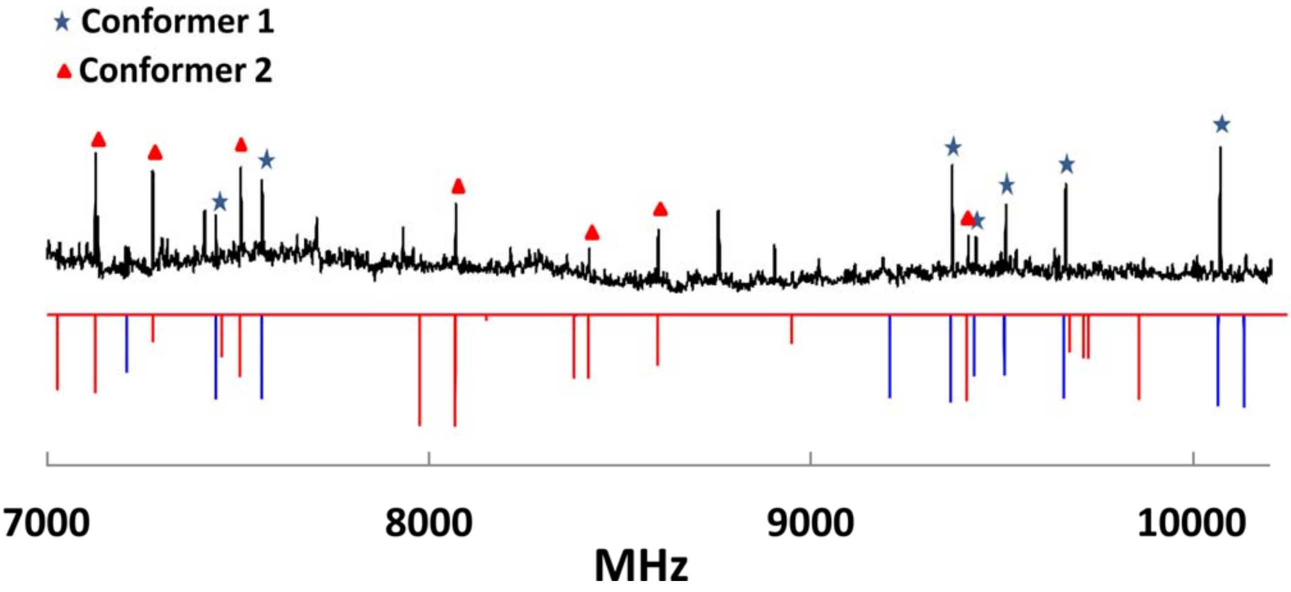


Table S1. Conformational search for methyl β-D-ribofuranoside.

Conformer[a]	**ΔG / kJ mol^{-1} (MP2/M06-2X/B3LYP)**[b]	***q* / Å**[c]	**φ / deg**	**μ_a / D**[d]	**μ_b / D**	**μ_c / D**	**μ_T / D**
1 ($^{3}T_{2}$)	0.0/0.0/0.0	0.385	264.7	0.0	-0.3	-1.2	1.2
2 ($^{3}T_{2}$)	0.8/1.2/0.9	0.397	260.7	-0.9	-3.5	-0.9	3.7
3 ($^{3}T_{2}$)	2.9/0.4/2.2	0.397	266.4	-1.6	-3.5	1.7	4.2
4 (E_{2})	3.5/4.6/2.9	0.400	252.3	1.3	-4.1	0.7	4.4
5 (^{2}E)	3.7/2.0/1.5	0.382	62.7	-2.1	-0.3	-0.5	2.1
6 (E_{2})	4.9/5.0/3.6	0.391	247.8	-0.9	-1.4	2.9	3.3
7 (E_{2})	6.2/5.5/3.6	0.391	247.3	-0.2	-0.2	-1.9	1.9
8 (^{4}E)	7.2/4.7/15.7	0.318	149.3	-0.2	0.3	-1.1	1.2
9 ($^{1}T_{2}$)	7.8/4.1/9.4	0.407	237.6	-1.4	-2.5	2.1	3.6
10 (E_{2})	7.8/7.7/6.1	0.375	254.8	0.9	1.4	-2.2	2.8
11 (^{4}E)	8.3/4.9/7.9	0.379	142.6	1.2	0.5	-2.8	3.1
12 (^{2}E)	9.5/10.3/5.9	0.396	68.6	3.0	-0.2	-0.9	3.1
13 ($^{3}T_{2}$)	9.9/9.0/8.0	0.414	265.7	3.9	1.9	0.2	4.4
14 (^{2}E)	12.1/14.6/9.0	0.381	70.2	-0.1	-1.7	0.5	1.8
15 ($^{3}T_{2}$)	12.1/12.2/11.0	0.396	265.2	2.4	-0.8	-0.1	2.6
16 (E_{2})	13.1/10.8/12.6	0.411	242.7	-2.3	-1.9	1.5	3.3
17 (^{4}E)	13.5/12.1/12.8	0.409	135.8	-0.9	-0.5	-0.7	1.3
18 ($^{4}T_{3}$)	14.6/14.9/10.0	0.367	130.9	-0.4	-1.0	1.1	1.6
19 (^{2}E)	14.7/15.8/10.9	0.390	75.7	1.4	-1.5	-1.8	2.8
20 (^{4}E)	15.0/14.9/11.4	0.353	134.7	-1.7	-2.4	0.2	2.9
21 (^{2}E)	15.1/15.4/10.1	0.393	71.4	1.9	-0.7	0.4	2.1
22 (^{4}E)	17.1/13.6/6.1	0.307	144.3	0.9	-0.9	-0.6	1.5
23 (^{4}E)	17.8/13.7/15.3	0.371	137.9	0.1	-0.1	1.2	1.2
24 ($^{4}T_{3}$)	18.1/13.7/6.1	0.332	134.1	1.7	0.2	0.7	1.9
25 ($^{2}T_{1}$)	18.9/18.1/18.9	0.409	57.5	-1.1	-1.0	0.8	1.7
26 ($^{4}T_{3}$)	19.6/15.4/16.5	0.331	129.3	1.6	1.7	-2.3	3.3
27 (^{2}E)	20.3/19.9/17.3	0.389	70.0	1.0	-2.3	2.1	3.3
28 (^{4}E)	22.7/18.5/18.4	0.373	136.6	-1.1	-1.1	-0.5	1.7
Neutron diffraction[e]							
Structure I (E_{2})		0.390	258.6				
Structure II (E_{2})		0.349	249.6				

[a] Conformer notation (see *Chem. Rev.*, **2013**, *113*, 1851; *Eur. J. Biochem.*, **1980**, *111*, 295; *Pure Appl. Chem.*, **1981**, *53*, 1901. The primed atom notation used in nucleosides is adopted for simplicity). [b] *Ab initio* calculations used the 6-311++G(d,p) basis set. Gibbs free energies relative to the minimum at 298 K and ΔG_0. [c] Cremer-Pople puckering parameters (*J. Am. Chem. Soc.*, **1975**, *97*, 1354). [d] Electric dipole moment components (μ_α, $\alpha = a, b, c$) and module (μ_T). [e] Calculated from crystal diffraction data (*Acta Crystallogr. B,* **2001**, *57*, 213; *J. Phys. Chem. A,* **1999**, *103*, 744).

Table S2. Rotational constants and predicted internal rotation barriers for conformers 1-6 of methyl-β-D-ribofuranoside (MP2/M06-2X/B3LYP values).

Conformer	**A /MHz**	**B /MHz**	**C /MHz**	**V_3 /kJ mol^{-1}**
1 ($^3T_2$)	1295.2/1332.4/1253.8	1101.1/1102.0/1068.3	718.9/728.4/682.9	7.90
2 ($^3T_2$)	1439.0/1463.6/1489.8	943.5/922.1/863.8	674.8/665.8/631.7	8.23
3 ($^3T_2$)	1285.6/1321.7/1241.6	1100.4/1101.3/1070.3	718.3/725.7/680.1	7.72
4 (E_2)	1161.4/1212.5/1117.5	1096.0/1079.9/1070.7	687.8/692.4/649.5	7.77
5 (^2E)	1273.1/1365.9/1250.3	1001.3/1060.3/988.1	716.9/778.9/693.3	8.02
6 (E_2)	1183.8/1250.5/1115.4	1093.7/1072.3/1088.7	689.2/696.3/652.4	8.43

Table S3. Rotational transitions (μ_c-type, Obs.) and residuals (o.-c.) of methyl-β-D-ribofuranoside conformer 1 (all frequencies in MHz).

J’	K'_{-1}	K'_{+1}	J’’	K''_{-1}	K''_{+1}	Sym	Obs.[a]	o.-c.[b]
3	2	1	2	1	1	A	6941.472	-0.005
						E	6941.472	0.001
3	1	2	2	0	2	A	6974.271	-0.001
						E	6974.271	0.004
3	3	0	2	2	0	A	7441.384	0.001
						E	7441.369	-0.002
3	3	1	2	2	1	A	7562.333	0.002
						E	7562.310	-0.001
4	2	2	3	1	2	A	9208.099	-0.004
						E	9208.099	0.001
4	3	1	3	2	1	A	9367.890	0.005
						E	9367.872	-0.001
4	1	3	3	0	3	A	9429.599	0.002
						E	9429.592	0.001
4	2	3	3	1	3	A	9508.127	0.001
						E	9508.109	-0.003
4	3	2	3	2	2	A	9663.945	0.003
						E	9663.920	-0.006
4	4	0	3	3	0	A	10068.685	-0.005
						E	10068.685	0.002
4	4	1	3	3	1	A	10136.000	0.002
						E	10135.960	0.002
5	2	3	4	1	3	A	11659.023	-0.003
						E	11659.023	0.004
5	1	4	4	0	4	A	11846.391	-0.002
						E	11846.391	-0.006
5	2	4	4	1	4	A	11865.074	0.006
						E	11865.041	-0.003
5	3	3	4	2	3	A	11890.550	-0.002
						E	11890.532	-0.002
5	4	1	4	3	1	A	11903.882	0.002
						E	11903.859	-0.002
5	4	2	4	3	2	A	12160.824	0.002
						E	12160.797	-0.002
5	5	0	4	4	0	A	12701.368	0.001
						E	12701.408	0.000
5	5	1	4	4	1	A	12730.227	-0.001
						E	12730.127	0.000
6	3	3	5	2	3	A	13843.928	-0.003
						E	13843.928	0.003
6	4	2	5	3	2	A	13865.094	0.002
						E	13865.076	-0.001
6	2	4	5	1	4	A	14133.338	0.001
						E	14133.324	-0.002
6	3	4	5	2	4	A	14209.761	0.001
						E	14209.741	-0.002

[a] Observed. [b] Observed minus calculated.

Table S4. Rotational transitions (μ_b-type, Obs.) and residuals (o.-c.) of methyl-β-D-ribofuranoside conformer 2 (all frequencies in MHz).

J’	**K'_{-1}**	**K'_{+1}**	**J’’**	**K''_{-1}**	**K''_{+1}**	**Sym**	**Obs.**[a]	**o.-c.**[b]
5	0	5	4	1	4	A	7026.421	-0.002
						E	7026.421	0.001
5	1	5	4	0	4	A	7125.994	-0.001
						E	7125.994	-0.001
5	1	4	4	2	3	A	7276.710	-0.002
						E	7276.710	0.002
4	2	3	3	1	2	A	7505.370	-0.002
						E	7505.370	0.003
3	3	1	2	2	0	A	7976.492	-0.008
						E	7976.475	-0.001
3	3	0	3	3	1	A	8069.047	0.009
						E	8069.047	0.002
6	0	6	5	1	5	A	8380.632	0.003
						E	8380.622	0.005
6	1	6	5	0	5	A	8417.751	0.001
						E	8417.751	-0.003
5	2	4	4	1	3	A	8600.021	-0.003
						E	8600.021	0.002
6	1	5	5	2	4	A	8950.963	-0.002
						E	8950.963	0.003
4	3	2	3	2	1	A	9409.592	0.002
						E	9409.577	-0.002
6	2	5	5	1	4	A	9679.330	-0.000
						E	9679.330	0.004
4	3	1	3	2	2	A	9860.614	-0.006
						E	9860.614	0.003
7	1	6	6	2	5	A	10473.037	0.001
						E	10473.029	-0.002
7	2	6	6	1	5	A	10819.490	-0.003
						E	10819.490	0.001

[a] Observed. [b] Observed minus calculated.

Table S5. MP2 structures for the two lowest energy conformers of methyl-β-D-ribofuranoside (6-311++G(d,p), principal axis system).

Atomic Number	Conformer 1			Conformer 2		
	***a*/Å**	***b*/Å**	***c*/Å**	***a*/Å**	***b*/Å**	***c*/Å**
6	-0.802038	-1.016844	0.296166	1.437161	0.285807	0.287024
6	0.517912	-1.365922	-0.369571	0.538631	1.363225	-0.298852
6	1.109570	0.028551	-0.583653	-0.715764	0.545779	-0.588675
6	0.682920	0.754519	0.690685	-0.763914	-0.383425	0.629873
8	-0.551882	0.135864	1.094052	0.590327	-0.560552	1.057301
8	1.298805	-2.095279	0.557759	0.290926	2.326698	0.706995
8	2.533088	0.010539	-0.666322	-1.837977	1.402532	-0.701238
6	0.446602	2.242087	0.515444	-1.389948	-1.722217	0.300921
8	-0.512642	2.506935	-0.495971	-2.698774	-1.402424	-0.188595
1	2.218346	-1.879024	0.353906	-0.584521	2.686497	0.514262
1	2.777489	0.097528	-1.591987	-2.613018	0.827755	-0.683457
1	0.360699	-1.925508	-1.297770	0.980347	1.811871	-1.194002
1	0.658219	0.504307	-1.459035	-0.567962	-0.035624	-1.506952
1	1.439111	0.582652	1.466974	-1.329573	0.107655	1.431114
1	0.137390	2.671246	1.477051	-0.788480	-2.219265	-0.470372
1	1.380049	2.718445	0.202161	-1.441500	-2.358415	1.191581
1	-1.283295	1.973310	-0.270174	-3.136517	-2.220278	-0.439328
8	-1.727368	-0.741554	-0.720913	2.014355	-0.399894	-0.791269
1	-1.171912	-1.803971	0.963848	2.204566	0.675084	0.966527
6	-3.037175	-0.525527	-0.205847	2.902315	-1.424747	-0.359145
1	-3.391497	-1.416056	0.328655	2.368381	-2.199274	0.199629
1	-3.061392	0.332249	0.474934	3.344111	-1.854052	-1.258573
1	-3.683118	-0.334479	-1.062865	3.695649	-1.004570	0.272774

Table S6. M062X structures for the two lowest energy conformers of methyl-β-D-ribofuranoside (6-311++G(d,p), principal axis system).

	Conformer 1			**Conformer 2**		
Atomic Number	***a*/Å**	***b*/Å**	***c*/Å**	***a*/Å**	***b*/Å**	***c*/Å**
6	-0.660874	-1.099921	0.289383	1.437606	0.290907	0.291646
6	0.684652	-1.281745	-0.395619	0.534095	1.364362	-0.299488
6	1.119958	0.177909	-0.568290	-0.721586	0.543839	-0.584772
6	0.585611	0.835844	0.707099	-0.758895	-0.389904	0.631806
8	-0.521655	0.030243	1.126851	0.591610	-0.565792	1.039494
8	1.548905	-1.949063	0.490803	0.280215	2.331229	0.690934
8	2.529780	0.318673	-0.619104	-1.844347	1.387802	-0.683627
6	0.103827	2.260019	0.505132	-1.394228	-1.723379	0.302689
8	-0.863526	2.340963	-0.519632	-2.688016	-1.399158	-0.199955
1	2.433074	-1.588569	0.352876	-0.597546	2.690848	0.516139
1	2.810179	0.409395	-1.532150	-2.626239	0.823361	-0.680169
1	0.576573	-1.820628	-1.341153	0.976395	1.803995	-1.196907
1	0.638098	0.615610	-1.445896	-0.577452	-0.034490	-1.504580
1	1.361421	0.803060	1.479142	-1.319039	0.100297	1.436046
1	-0.291690	2.640501	1.453834	-0.788025	-2.229862	-0.457990
1	0.946068	2.887370	0.203748	-1.458034	-2.355629	1.193440
1	-1.520389	1.655323	-0.352141	-3.162172	-2.201892	-0.424485
8	-1.619180	-0.868488	-0.703197	2.030603	-0.388149	-0.774414
1	-0.942004	-1.949524	0.919503	2.192629	0.686086	0.978866
6	-2.941542	-0.823714	-0.197209	2.903770	-1.421137	-0.360015
1	-3.219668	-1.789804	0.238569	2.360999	-2.197617	0.185129
1	-3.046972	-0.046309	0.566329	3.346174	-1.843590	-1.260334
1	-3.597833	-0.604517	-1.037414	3.697853	-1.020520	0.281232

Table S7. B3LYP structures for the two lowest energy conformers of methyl-β-D-ribofuranoside (6-311++G(d,p), principal axis system).

	Conformer 1			**Conformer 2**		
Atomic Number	***a*/Å**	***b*/Å**	***c*/Å**	***a*/Å**	***b*/Å**	***c*/Å**
6	-1.034772	-0.779509	0.305113	1.440251	0.220253	0.314036
6	0.170703	-1.430069	-0.373800	0.563948	1.333558	-0.263979
6	1.121666	-0.233169	-0.556854	-0.725486	0.570141	-0.588760
6	0.842192	0.613737	0.690168	-0.805445	-0.428791	0.576734
8	-0.533311	0.350631	1.025726	0.550545	-0.719972	0.929793
8	0.731089	-2.384322	0.512358	0.342949	2.306194	0.744077
8	2.494400	-0.629714	-0.580992	-1.820048	1.469060	-0.660969
6	1.028023	2.112594	0.508610	-1.541611	-1.710362	0.225960
8	0.249524	2.635361	-0.558959	-2.859921	-1.300398	-0.170524
1	1.686866	-2.378875	0.363978	-0.524875	2.695764	0.572717
1	2.804252	-0.647822	-1.491102	-2.628304	0.940493	-0.660244
1	-0.123392	-1.894677	-1.319911	1.030268	1.776456	-1.148283
1	0.857570	0.327175	-1.456459	-0.597045	0.035668	-1.537490
1	1.486110	0.267044	1.507496	-1.305615	0.055510	1.423834
1	0.790855	2.618828	1.452772	-1.024014	-2.220056	-0.595425
1	2.073612	2.318182	0.266619	-1.580508	-2.379506	1.092175
1	-0.667736	2.387715	-0.391975	-3.384316	-2.072912	-0.398658
8	-1.945843	-0.384557	-0.685153	2.153993	-0.366712	-0.739678
1	-1.514332	-1.447128	1.028912	2.120885	0.581428	1.092577
6	-3.189884	0.084852	-0.173407	3.071813	-1.374508	-0.328019
1	-3.678094	-0.689616	0.431425	2.552128	-2.222727	0.126769
1	-3.058924	0.983785	0.437114	3.596727	-1.704228	-1.224093
1	-3.815854	0.316761	-1.034369	3.798347	-0.970159	0.388596

Table S8. Most relevant hyperconjugation energies (E_2, kcal/mol) between the lone pairs of the oxygen atoms $O_{1'}$ and $O_{4'}$ and the vicinal σ*(C-O) orbitals of methyl-β-D-ribofuranoside according to a Natural Bond Orbital calculation (B3LYP/6-311++G(d,p)).

Conformer	*endo* LP(2) $O_{1'}$– σ*($C_{1'}$-$O_{4'}$)	*exo* LP(2) $O_{4'}$ – σ*($C_{1'}$-$O_{1'}$)
1 ($^3T_2$)	14.22	11.93
2 ($^3T_2$)	13.33	13.61
3 ($^3T_2$)	13.62	13.37
4 (E_2)	12.79	14.61
5 (^2E)	14.61	3.90
6 (E_2)	14.31	5.77