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DFT study of α- and β-D-allopyranose at the B3LYP/6-311++G** level of theory

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Abstract—One hundred and two conformations of α- and β-D-allopyranose, the C-3 substituted epimer of glucopyranose, were geometry optimized using the density functional, B3LYP, and the basis set, 6-311++G**. Full geometry optimization was performed on different ring geometries and on the hydroxymethyl rotamers (*gg*/*gt*/*tg*). Analytically derived Hessians were used to calculate zero point energy, enthalpy, and entropy. The lowest energy and free energy conformation found is the α-*tg*(*g*−)-$^4C_1$-*c* conformation, which is only slightly higher in electronic (∼0.2 kcal/mol) and free energy than the lowest energy α-D-glucopyranose. The in vacuo calculations showed a small (∼0.3 kcal/mol) energetic preference for the α- over the β-anomer for allopyranose in the $^4C_1$ conformation, whereas in the $^1C_4$ conformation a considerable (∼1.6 kcal/mol) energetic preference for the β- over the α-anomer for allopyranose was encountered. The results are compared to previous aldohexose calculations in vacuo. Boat and skew forms were found that remained stable upon gradient optimization although many starting boat conformations moved to other skew forms upon optimization. As found for glucose, mannose, and galactose the orientation and interaction of the hydroxyl groups make the most significant contributions to the conformation/energy relationship in vacuo. A comparison of different basis sets and density functionals is made in the Discussion section, confirming the appropriateness of the level of theory used here.
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1. Introduction

1.1. Background

Allopyranose (allose) is a rare aldohexose, which has lately gained attention for a variety of uses, namely, as a potential cancer inhibitor,[1,2] a sweetener,[3] and as use as a bulk agent.[4] For example, it was recently shown that D-allose has a significant inhibitory effect on ovarian cancer cell production.[1] Such studies were only recently possible because of the progress made in synthesizing large quantities of rare sugars via enzymatic reactions[5–7] instead of the costly cyanohydrin reaction.[8,9] Allopyranose is extremely rare in nature but is found in the leaves of the passion fruit plant in the form of benzylic β-D-allopyranosides.[10]

The conformational preferences of allose and its derivatives have been probed experimentally by NMR[11–14] studies, Vibrational Raman Optical Activity (ROA),[15] and Vibrational Circular Dichroism (VCD)[16] measurements, and X-ray crystal structure.[17] In the crystalline form, the β-*gg*-$^4C_1$ conformation is found, in which all hydroxyl groups act as proton donors and acceptors, except for the C-3 hydroxyl, which acts only as a donor. NMR studies[11–14] show that α- and β-D-allose prefer the $^4C_1$ conformation in aqueous solution with preference given to the β-anomer with an α/β-anomeric ratio reported to be ∼15/85%.[11,18]

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† Names are necessary to report factually on available data; however, the USDA neither guarantees nor warrants the standard of the product, and the use of the name by USDA implies no approval of the product to the exclusion of others that may also be suitable.

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A computational study of allose of this scope and at this level of theory has not been reported although specific $^4C_1$ conformations have been studied at a level of theory similar to that used here.[19,20] Empirical potentials have previously been used by Dowd[21] and Damm[22] to study glucose epimers including D-allopyranose;[21] unfortunately, the results in Dowd's paper were not presented in sufficient detail (i.e., the hydroxyl groups rotation and hydroxymethyl conformations were not included in the table of energies, nor were internal coordinates) to make either energy or structural comparisons to our results. A comparison with Damm's[22] work will be presented in the Discussion section, along with a description of the effect of hydration on the α/β anomeric ratio. In addition, relative energy differences between nine different Pople basis sets and different density functionals are included in the Discussion section.

This work is a continuation study of the structure and energetics of epimers of glucose from this laboratory. Standard density functional methods are applied to the structural study of the $^4C_1$ and $^1C_4$ conformations as well as boat and skew conformations of α- and β-D-allose. The driving force behind this study is to investigate the effects of epimerization at the C-3 position on the energy/property relationships of the pyranose carbohydrates, and apply these relationships in the design of new carbohydrate polymers with desired properties.

Previous DFT calculations from this laboratory on glucose,[23] mannose,[24] and galactose[25] are briefly compared with the allose results as are specific experimental/computational studies in which structural or energetic material is presented.

2. Methodology

2.1. Computational methods

The initial chair, boat, and skew conformations were constructed using constraining potentials on ring dihedral angles, different low energy combinations of hydroxyl and hydroxymethyl group orientations, and briefly

Table 1. Calculated[a] and ideal[b] improper dihedral angles for D-allopyranose ring conformations[c]

Conformations		Improper dihedrals[d]			Puckering parameters[e]			Pattern
		α1	α2	α3	Q	ϕ	θ	
Alpha	$^4C_1$	−33.1	−29.7	−31.8	0.549	3–320	4.2	
Beta		−36.3	−26.2	−35.1	0.568	1–349	6.7	
Ideal		−35.0	−35.0	−35.0		0–360	0.0	'− − −'
Alpha	$^1C_4$	33.5	30.6	27.3	0.529	218–335	174.7	
Beta		28.9	33.6	25.8	0.510	5–352	172.8	
Ideal		35.0	35.0	35.0		0–360	180.0	'+ + +'
Alpha	$^1S_3$	58.6	−53.1	−2.9	0.735	213.9	89.0	
Beta		42.7	−54.3	−0.8	0.643	206.3	81.7	
Ideal		60.0	−60.0	0.0		210.0	90.0	'+ − 0'
Beta	$^1S_5$	51.4	3.1	−55.4	0.712	273.6	89.0	
Ideal		60.0	0.0	−60.0		270.0	90.0	'+ 0 −'
Beta	$^3S_1$	−62.1	45.8	−1.3	0.713	35.1	84.4	
Ideal		−60.0	60.0	0.0		30.0	90.0	'− + 0'
Alpha	$^OS_2$	−4.0	56.1	−55.1	0.736	331.5	90.4	
Beta		−12.6	62.7	−50.1	0.751	340.4	91.6	
Ideal		0.0	60.0	−60.0		330.0	90.0	'0 + −'
Beta	^2S_O	2.5	−55.9	39.4	0.646	157.2	81.4	
Ideal		0.0	−60.0	60.0		150.0	90.0	'0 − +'
Alpha	$^{1,4}B$	61.0	−39.9	−21.5	0.711	230.6	87.9	
Ideal		60.0	−30.0	−30.0		240.0	90.0	'+ − −'
Beta	$B_{1,4}$	−65.6	33.1	10.9	0.697	48.4	82.3	
Ideal		−60.0	30.0	30.0		60.0	90.0	'− + +'
Alpha	$B_{2,5}$	34.8	12.3	−62.7	0.698	287.5	83.1	
Ideal		30.0	30.0	−60.0		300.0	90.0	'+ + −'
Beta	$B_{3,O}$	16.1	−64.4	32.3	0.690	170.7	81.3	
Ideal		30.0	−60.0	30.0		180.0	90.0	'+ − +'

[a] The listed values represent averaged values where possible.
[b] The ideal improper dihedral angles were taken from Ref. 38.
[c] All dihedral angles are in degrees.
[d] The improper dihedrals are defined as α1 = C4–O5–C2–C1, α2 = O5–C2–C4–C3, α3 = C2–C4–O5–C5.
[e] The Cremer–Pople puckering parameter Q is in Å and the angles ϕ and θ are in degrees.

Table 2. Hydroxyl orientations, improper dihedral angles, and relative electronic energies ΔE (kcal/mol) and free energies ΔG^0_{298}(kcal/mol)[a] for geometry optimized chair forms of D-allopyranose[b]

Geometry optimized conformations[c]	Starting conformations[d]	Hydroxy methyl orientation (C5–C6–O6–H)	Hydroxyl orientation[e] (C1,C2,C3,C4)	Improper dihedrals[f]			Cremer–Pople puckering parameters[g]			ΔE	$\Delta(\Delta G^0_{298})$
				α1	α2	α3	Q	ϕ	θ		
α-*gg*-$^4C_1$		*g*+	*rcrr*	−33.81	−30.73	−28.07	0.534	105.1	3.8	0.393	0.924
α-*gg*-$^4C_1$		*g*+	*c*0*cc*	−34.25	−30.51	−31.43	0.561	57.9	2.5	0.647	0.441
α-*gg*-$^4C_1$	α-*gg*-$B_{3,O}$	*g*−	*rcrr*	−32.82	−31.09	−30.86	0.547	137.7	1.0	2.561	2.783
α-*gg*-$^4C_1$		*t*	*rcrr*	−33.75	−30.97	−28.17	0.534	110.9	3.7	2.769	2.717
α-*gg*-$^4C_1$		*t*	*c*0*cc*	−33.71	−30.86	−33.10	0.568	20.5	1.4	3.053	2.326
α-*gg*-$^4C_1$		*g*−	*crcc*	−34.40	−30.78	−30.73	0.558	74.6	2.9	6.459	5.773
α-*gt*-$^4C_1$	α-*tg*-$^4C_1$	*g*−	*rcrr*	−33.89	−30.22	−30.12	0.544	78.7	2.2	0.335	0.816
α-*gt*-$^4C_1$		*g*−	*c*0*cc*	−34.16	−30.75	−31.37	0.562	62.3	2.6	1.960	1.897
α-*gt*-$^4C_1$	α-*tg*-$^4C_1$	*t*	*rcrr*	−33.78	−30.09	−31.06	0.547	56.6	1.6	2.455	2.433
α-*gt*-$^4C_1$		*g*+	*rcrr*	−33.79	−30.24	−29.92	0.541	84.4	2.2	2.932	2.882
α-*gt*-$^4C_1$		*g*+	*c*0*cc*	−35.07	−29.81	−31.31	0.560	52.9	3.7	5.720	4.800
α-*tg*-$^4C_1$		*g*−	*c*0*cc*	−35.04	−29.95	−31.39	0.560	57.2	3.6	0.000	0.732
α-*tg*-$^4C_1$		*g*+	*crrr*	−31.61	−29.48	−33.23	0.546	316.6	2.4	1.724	2.578
α-*tg*-$^4C_1$		*g*+	*rrrr*	−25.05	−24.39	−40.08	0.530	296.2	13.6	2.164	2.559
α-*tg*-$^4C_1$		*t*	*cccc*	−28.93	−21.51	−40.22	0.534	319.9	13.4	3.065	3.067
α-*tg*-$^4C_1$	α-*gt*-$^4C_1$	*g*+	*crcr*	−33.02	−31.24	−33.20	0.566	2.6	7.1	3.326	2.574
β-*gg*-$^4C_1$		*g*+	*rrrr*	−37.11	−27.33	−31.63	0.554	35.0	5.9	0.253	0.065
β-*gg*-$^4C_1$		*g*−	*rrrr*	−35.89	−27.29	−34.61	0.568	4.9	5.3	3.082	2.315
β-*gg*-$^4C_1$		*g*+	*cccc*	−36.46	−25.75	−35.36	0.570	341.3	0.8	3.326	3.899
β-*gg*-$^4C_1$		*t*	*cccc*	−34.05	−26.47	−38.32	0.578	338.1	7.6	5.750	4.205
β-*gg*-$^4C_1$		*g*−	0*ccc*	−35.79	−27.09	−34.33	0.567	12.4	6.1	9.314	7.312
β-*gt*-$^4C_1$		*g*−	*rrrr*	−37.53	−26.05	−34.09	0.566	15.6	7.2	0.294	0.000
β-*gt*-$^4C_1$		*t*	*rrrr*	−37.48	−26.22	−33.73	0.566	19.0	7.0	3.842	2.791
β-*gt*-$^4C_1$		*g*+	*rrrr*	−37.73	−26.41	−32.45	0.560	29.5	7.0	3.957	2.907
β-*gt*-$^4C_1$		*g*−	*cccc*	−37.38	−25.22	−35.46	0.571	7.4	8.0	4.512	3.712
β-*gt*-$^4C_1$		*g*−	*cc*0*r*	−35.57	−26.04	−35.06	0.564	5.8	7.1	6.956	6.408
β-*gt*-$^4C_1$		*g*+	0*ccc*	−36.39	−25.97	−34.98	0.569	9.7	7.5	8.477	6.492
β-*gt*-$^4C_1$		*t*	*cc*0*r*	−33.86	−26.68	−37.84	0.576	337.4	7.2	11.81	9.575
β-*tg*-$^4C_1$		*g*+	*rrrr*	−36.78	−25.64	−35.55	0.569	0.9	7.3	0.488	0.636
β-*tg*-$^4C_1$		*t*	*cccc*	−38.05	−24.97	−34.53	0.565	16.5	8.2	2.665	2.663
β-*tg*-$^4C_1$		*g*−	*cccc*	−35.80	−26.04	−35.30	0.566	6.7	7.2	3.062	2.026
β-*tg*-$^4C_1$	α-*gt*-$^4C_1$	*g*+	0*ccr*	−35.05	−26.33	−37.09	0.579	348.6	7.3	6.006	5.573
α-*gg*-$^1C_4$	α-*gg*-(*g*+)-$^1C_4$	*t*	*ccrr*	35.26	28.31	25.97	0.523	261.9	172.4	3.961	4.518
α-*gg*-$^1C_4$	α-*gg*-(*g*+)-$^1C_4$	*t*	*rrcr*	33.10	33.44	24.82	0.530	312.6	172.5	4.275	4.379
α-*gg*-$^1C_4$	α-*gg*-(*g*+)-$^1C_4$	*t*	*ccc*0	32.67	28.46	28.61	0.520	254.5	176.6	4.353	4.674
α-*gg*-$^1C_4$		*t*	*ccrc*	32.67	31.67	27.07	0.533	297.7	174.8	5.848	5.929
α-*gg*-$^1C_4$	α-*gg*-(*g*+)-$^1C_4$	*t*	*rrrr*	33.75	22.96	27.24	0.475	217.9	172.4	8.197	7.572
α-*gg*-$^1C_4$	α-*gg*-(*g*+)-$^1C_4$	*t*	*cccc*	33.69	23.86	27.13	0.485	228.0	172.1	10.02	9.297
α-*gt*-$^1C_4$		*g*−	*ccc*0	32.96	29.04	29.19	0.527	256.1	177.0	4.202	4.693
α-*gt*-$^1C_4$		*g*−	*rrcr*	32.87	33.85	25.81	0.535	318.3	173.2	4.763	4.804
α-*gt*-$^1C_4$		*g*−	*ccrc*	32.53	32.22	28.25	0.540	305.3	175.7	4.979	5.256
α-*gt*-$^1C_4$		*g*+	*rrcr*	34.25	31.69	29.50	0.549	291.8	176.9	5.839	5.567
α-*gt*-$^1C_4$		*t*	*rrcr*	33.75	32.05	28.97	0.546	304.3	176.8	6.515	6.201
α-*gt*-$^1C_4$		*t*	*ccrc*	31.52	31.71	31.03	0.546	335.4	178.5	8.361	7.902
α-*tg*-$^1C_4$		*g*−	*ccrr*	34.11	29.58	27.70	0.529	269.4	174.7	5.383	5.689
α-*tg*-$^1C_4$		*t*	*ccrr*	33.33	30.15	27.86	0.529	278.8	175.4	5.474	5.612
α-*tg*-$^1C_4$	α-*gt*-$^1C_4$	*g*+	*rrcr*	33.07	33.38	27.15	0.540	318.1	174.7	6.736	6.480
α-*tg*-$^1C_4$		*g*+	*ccc*0	32.55	28.58	30.72	0.531	221.9	177.9	7.091	6.965
α-*tg*-$^1C_4$		*g*−	*cccr*	35.36	32.93	24.44	0.541	290.7	170.9	7.925	8.009
α-*tg*-$^1C_4$		*g*+	*cccr*	36.00	32.28	24.80	0.544	284.6	171.2	10.14	9.498
β-*gg*-$^1C_4$		*g*+	*rcc*0	25.66	30.11	28.03	0.483	33.3	174.7	2.601	3.898
β-*gg*-$^1C_4$		*g*+	*rcrc*	26.51	33.80	26.36	0.504	5.1	172.0	4.070	4.941
β-*gg*-$^1C_4$		*g*+	*rrcr*	27.38	34.01	24.57	0.500	351.1	171.3	4.645	5.225
β-*gg*-$^1C_4$		*t*	*rrcr*	28.98	34.51	23.19	0.509	332.1	170.3	5.008	5.872
β-*gg*-$^1C_4$		*g*−	*rcc*0	28.86	31.58	25.37	0.500	331.6	174.1	5.780	6.492
β-*gg*-$^1C_4$		*t*	*rcrc*	27.97	33.43	25.75	0.509	344.8	172.9	6.411	7.133
β-*gg*-$^1C_4$		*g*−	*rrcr*	29.66	34.32	23.27	0.512	328.3	170.6	6.433	6.917
β-*gg*-$^1C_4$		*g*−	*rcrc*	28.29	33.12	26.33	0.512	344.9	173.6	7.979	8.461
β-*gt*-$^1C_4$		*g*−	*rcc*0	28.05	33.09	24.54	0.496	343.8	172.2	4.903	5.145

Table 2 (*continued*)

Geometry optimized conformations[c]	Starting conformations[d]	Hydroxy methyl orientation (C5–C6–O6–H)	Hydroxyl orientation[e] (C1,C2,C3,C4)	Improper dihedrals[f]			Cremer–Pople puckering parameters[g]			ΔE	$\Delta(\Delta G^0_{298})$
				α1	α2	α3	Q	ϕ	θ		
β-*gt*-$^1C_4$		*g*+	*rrcr*	31.49	32.78	27.76	0.530	329.0	175.5	5.863	6.083
β-*gt*-$^1C_4$		*g*−	*rcrc*	27.55	35.62	25.10	0.514	351.7	170.5	6.016	5.935
β-*gt*-$^1C_4$		*g*−	*rrcr*	29.50	36.15	21.60	0.512	332.4	168.1	6.253	6.043
β-*gt*-$^1C_4$		*g*+	*rcrc*	31.01	32.56	28.56	0.531	338.2	176.2	6.764	6.585
β-*gt*-$^1C_4$		*t*	*rrcr*	30.39	32.44	28.70	0.527	350.5	176.3	7.163	7.069
β-*tg*-$^1C_4$		*g*−	*rcrr*	30.24	32.02	25.16	0.503	326.4	173.6	4.707	5.107
β-*tg*-$^1C_4$		*t*	*rcrr*	29.25	32.38	25.86	0.503	339.6	173.9	4.851	5.039
β-*tg*-$^1C_4$		*t*	*rcrc*	28.93	34.59	26.09	0.518	347.6	172.3	5.797	5.499
β-*tg*-$^1C_4$		*g*−	*rcrc*	29.33	34.58	25.88	0.519	343.9	172.3	6.411	6.015
β-*tg*-$^1C_4$		*g*+	*rrcr*	29.23	34.96	25.13	0.518	343.5	171.6	7.498	6.994
β-*tg*-$^1C_4$		*g*−	*c0rr*	30.04	31.62	25.35	0.503	322.1	174.0	9.333	9.232

[a] $\Delta G^0_{298} = E + (H - TS) + RT$.
[b] All dihedral angles are in degrees.
[c] B3LYP/6-311++G** optimized geometries.
[d] Starting conformations are the same as the optimized geometries unless noted otherwise.
[e] Orientation of the hydroxyl groups in the 1-, 2-, 3-, and 4-positions: a clockwise orientation is marked as '*c*' and a counter clockwise direction is marked as '*r*', the marking '0' indicates a trans direction relative to the methine hydrogen between '*c*' and '*r*'.
[f] The improper dihedrals are defined as α1 = C4–O5–C2–C1, α2 = O5–C2–C4–C3, α3 = C2–C4–O5–C5.
[g] The Cremer–Pople puckering parameter Q is in Å and the angles ϕ and θ are in degrees.

pre-optimized (PM3) under constraints using HyperChem v7.5.[26] The generated initial conformations were examined to confirm the correct conformation with no high energy contacts, and then fully optimized using the B3LYP non-local exchange functionals with the 6-31+G* and subsequently 6-311++G** basis sets as described previously by this group.[23–25,27,28] Other groups have used these large basis sets in their DFT investigations of carbohydrates.[29–31] Convergence criteria for the optimization were set at 1×10^{-6} Hartree for the energy and a gradient of less than 3×10^{-4} a.u. To ensure that the geometry optimized conformations are at local minima, vibrational frequencies (not presented here) were calculated using an analytical Hessian, which provided zero point vibrational energies (ZPVE), enthalpies (H), and entropies (S). DFT in vacuo studies from this laboratory on monosaccharides,[23–25] disaccharides,[27,28,32] and explicitly hydrated glucose[33,34] and cellobiose[35,36] have shown that the B3LYP/6-311++G** level of theory will give consistently reliable geometries, conformations, and energies for carbohydrates. For this reason, all allose structures reported here are at the B3LYP/6-311++G** level of theory, although the smaller basis set optimized structures are directly compared to the larger set structures in the discussion. The DFT calculations were carried out on Parallel Quantum Solutions software and hardware.[37] The results have been displayed using HyperChem v7.5.[26]

2.2. Nomenclature and conventions

The standard numbering scheme is used for the pyranose ring.[38,39] The geometric assignments of the chair, boat, and skew forms were made using improper dihedral angles as described previously.[23,38,40] It should be noted here that using improper dihedrals for the conformational assignment can still be difficult because the improper dihedral angles can differ significantly from the ideal improper dihedrals (see Table 1). Another way to consider the conformational assignment is by using a '+/−' pattern of the improper dihedrals, for example, for the $^4C_1$ conformation the pattern would be '− − −' as shown in Table 1. The pattern for each of the conformations is unique to the ring conformation. Still when one of the ideal improper dihedral angles is close to zero (all of the skew conformations), a tolerance of +/−10° was imposed to allow or disallow a particular assignment. The addition of the Cremer–Pople[41] puckering parameters to Tables 1–3 allows analysis for those familiar with these parameters.

The different rotamer conformations of the hydroxymethyl are denoted by:

tg	O6 is trans to the ring oxygen O5 (O5–C5–C6–O6 dihedral ∼180°)
gg	C6–O6 bond is gauche to the C5–O5 and C5–C4 bonds (O5–C5–C6–O6 dihedral <0°)
gt	C6–O6 bond is gauche to the C5–O5 bond and trans to the C5–C4 bond (O5–C5–C6–O6 dihedral >0°)

In this study, the orientations of the hydroxyl groups in the 1-, 2-, 3-, and 4-positions are defined by this

Table 3. Hydroxyl orientations, improper dihedral angles, and relative electronic energies ΔE (kcal/mol) and free energies ΔG^0_{298} (kcal/mol)[a] for geometry optimized boat and skew forms of D-allopyranose[b]

Geometry optimized conformations[c]	Starting conformations[d]	Hydroxy methyl orientation (C5–C6–O6–H)	Hydroxyl orientation[e] (C1,C2,C3,C4)	Improper dihedrals[f]			Cremer–Pople puckering parameters[g]			ΔE	$\Delta(\Delta G^0_{298})$
				α1	α2	α3	Q	ϕ	θ		
α-*gg*-$^{1,4}B$		*g*+	*cccc*	60.96	−39.89	−21.50	0.711	230.6	87.9	8.797	7.595
α-*tg*-$B_{2,5}$		*g*+	*rrrr*	34.81	12.31	−62.70	0.698	287.5	83.1	6.017	5.922
β-*gg*-$B_{1,4}$		*g*+	*rrrr*	−65.58	33.11	10.87	0.697	48.4	82.3	8.119	7.210
β-*gg*-$B_{3,O}$		*g*+	*cc0r*	18.26	−63.68	30.18	0.676	172.6	81.7	8.555	8.487
β-*gg*-$B_{3,O}$	β-*gg*-(*g*−)-$B_{3,O}$	*t*	*0rrr*	13.85	−65.18	34.48	0.705	168.8	80.9	9.061	9.660
α-*gg*-$^{1}S_3$	α-*gg*-$^{1,4}B$	*t*	*rrrr*	59.83	−49.09	−6.32	0.715	217.4	89.4	7.534	6.995
α-*gt*-$^{1}S_3$	α-*gt*-$B_{3,O}$	*g*−	*rrrr*	59.64	−48.37	−7.45	0.710	218.1	89.1	8.082	7.357
α-*tg*-$^{1}S_3$	α-*tg*-$B_{3,O}$	*g*+	*cc0r*	56.36	−61.72	5.17	0.780	206.4	88.6	9.561	10.24
β-*gg*-$^{1}S_3$	β-*gg*-$^{1,4}B$	*g*+	*rccc*	42.70	−54.33	−0.82	0.643	206.3	81.7	7.850	6.471
β-*gg*-$^{1}S_5$	β-*gg*-$B_{2,5}$	*g*+	*rccc*	50.20	4.44	−57.39	0.720	275.5	88.4	5.999	5.451
β-*gg*-$^{1}S_5$	β-*gg*-$B_{2,5}$	*g*+	*rccc*	50.19	4.45	−57.44	0.720	275.5	88.4	6.006	5.380
β-*gg*-$^{1}S_5$	β-*gg*-$B_{2,5}$	*g*+	*rrrr*	52.08	3.15	−53.67	0.703	272.8	90.1	8.137	7.644
β-*gt*-$^{1}S_5$	β-*gt*-$B_{2,5}$	*g*−	*rrrr*	52.06	2.28	−54.01	0.706	272.4	89.5	7.744	7.145
β-*tg*-$^{1}S_5$	β-*tg*-$B_{2,5}$	*g*+	*rrrr*	52.63	1.16	−54.57	0.712	271.9	88.9	6.916	7.015
β-*gg*-$^{3}S_1$	β-*gg*-$^{3,O}B$	*g*+	*rrrr*	−62.51	43.32	0.79	0.703	37.3	84.0	6.715	5.830
β-*gt*-$^{3}S_1$	β-*gt*-$^{3,O}B$	*g*−	*rrrr*	−61.79	48.37	−3.43	0.723	32.9	84.7	6.928	5.979
β-*gg*-$^{3}S_1$		*g*+	*c0rr*	−49.48	59.99	−18.21	0.732	16.3	88.7	9.599	8.778
α-*gg*-$^{O}S_2$	α-*gg*-$B_{2,5}$	*g*+	*rrc0*	−3.10	61.91	−50.73	0.748	334.3	95.0	3.284	3.826
α-*gg*-$^{O}S_2$	α-*gg*-$B_{2,5}$	*g*+	*cccc*	1.28	47.95	−60.63	0.720	323.9	86.7	5.657	5.149
α-*gg*-$^{O}S_2$	α-*gg*-$B_{1,4}$	*g*+	*cccc*	1.56	47.71	−60.72	0.719	323.7	86.7	5.668	5.110
α-*gg*-$^{O}S_2$		*g*+	*cccc*	−10.95	63.47	−49.72	0.752	339.6	92.7	5.855	5.844
α-*gt*-$^{O}S_2$		*g*−	*cccc*	−11.08	63.83	−49.57	0.753	339.9	92.9	6.164	6.258
α-*gg*-$^{O}S_2$	α-*gg*-$B_{2,5}$	*t*	*ccc0*	−8.99	59.96	−51.73	0.736	337.0	91.5	7.343	11.31
α-*gt*-$^{O}S_2$	α-*gt*-$^{3,O}B$	*g*−	*rrc0*	−4.60	62.75	−51.08	0.756	335.3	94.6	3.343	3.756
α-*gt*-$^{O}S_2$		*g*−	*cccc*	−0.66	50.49	−59.95	0.726	326.2	87.3	6.480	5.692
α-*tg*-$^{O}S_2$	α-*tg*-$^{1,4}B$	*t*	*cccc*	0.99	46.97	−61.39	0.715	323.8	86.1	5.136	4.720
β-*gg*-$^{O}S_2$		*g*+	*rcc0*	−17.21	61.19	−47.47	0.731	343.8	90.0	6.056	5.643
β-*gt*-$^{O}S_2$		*g*+	*rrc0*	−11.02	63.65	−51.66	0.764	339.0	92.1	9.370	8.086
β-*gg*-$^{O}S_2$	β-*gg*-$^{3,O}B$	*g*−	*rrc0*	−9.69	63.27	−51.11	0.758	338.4	92.7	10.27	8.679
β-*gg*-$^{2}S_O$	β-*gg*-$B_{3,O}$	*g*+	*rrrr*	4.93	−57.03	36.13	0.638	160.4	80.4	6.545	6.711
β-*gg*-$^{2}S_O$	β-*gg*-$^{1,4}B$	*g*+	*rrrr*	5.02	−57.05	36.13	0.638	160.4	80.5	6.567	6.621
β-*tg*-$^{2}S_O$	β-*tg*-$B_{3,O}$	*g*−	*rrrr*	−2.33	−53.75	45.93	0.662	150.8	83.4	10.09	9.366

[a–g] See legends in Table 2.

orientation relative to the O5 ring oxygen. The notion used is '*c*' for clockwise and '*r*' for counter clockwise orientation. In some cases it was necessary to use the label zero '0' to indicate that the orientation was neither '*c*' nor '*r*', found here to be most often trans to the methine hydrogen. The full definition of every hydroxyl orientation (*r*, *c*, or 0) can be found for each structure in Tables 2 and 3. In addition, the specific orientation of the H–O6 hydroxyl group is specified by the value of the C5–C6–O6–H dihedral angle as follows: *g*+ (C5–C6–O6–H dihedral >0°), *g*− (C5–C6–O6–H dihedral <0°), and *t* (C5–C6–O6–H dihedral ~180°). This addition to the notation was needed because the orientation of the H–O6 hydroxyl group with respect to the O5 ring oxygen is of energetic importance, for example, the energy difference between a *gg*-(*g*+) and a *gg*-(*g*−) conformation can be on the order of 1–2 kcal/mol.

3. Results

3.1. Conformations

In the present work, 102 unique allopyranose conformations have been found. The B3LYP/6-311++G** optimized conformations and relative energies are listed in Tables 2 and 3 together with the assignment of the hydroxyl orientations and the improper dihedral angles. The $^4C_1$ conformations have relative electronic energies in the range of 0 → 11 kcal/mol and a relative free energy range of 0 → 9 kcal/mol. Similarly, the $^1C_4$ conformations have a relative energy of ~3 → 10 kcal/mol and relative free energy range of ~3 → 9 kcal/mol. The stable boat and skew forms examined are ~4–11 kcal/mol higher in energy than the lowest energy $^4C_1$ conformer, but only ~1–7 kcal/mol higher in energy than the lowest energy $^1C_4$ conformer. Of the boat conformations exam-

ined (see Table 3 under *Starting conformations*), the $B_{2,5}$ conformer formed the most stable boat form. Many other starting boat conformations optimized to stable skew forms as shown in Tables 2 and 3. In agreement with our previous studies[23–25] of epimers of D-glucopyranose, the $^4C_1$ conformation is energetically preferred.

3.2. $^4C_1$ Chairs: general remarks

Selected calculations for the vacuum $^4C_1$ conformations of α- and β-D-allopyranose rotamers are presented in Tables 4 and 5 (see also Figs. 1 and 2), respectively. Anomeric effects, rotamer conformations, and the orientation of the hydroxyls (with an emphasis on the C-3 hydroxyl orientation) are the focus of the $^4C_1$ conformational investigations. In the case of glucopyranose, the α-*gt*(*g*−)-$^4C_1$-*r* conformation was of lowest energy, while in the allopyranose structures studied here, the α-*tg*(*g*−)-$^4C_1$-*c* conformation has the lowest energy. Interestingly, the allose electronic energy of α-*tg*(*g*−)-$^4C_1$-*c* is only slightly higher than the best structure found for glucose (~0.2 kcal/mol) but is ~0.6 kcal/mol lower in energy than the lowest energy mannose conformation using the same DFT methods and basis set. The resulting

Table 4. Geometry optimized B3LYP/6-311++G** energies (*E*), harmonic zero point vibrational energies (ZPVE), enthalpies (*H*), entropies (*S*), free energies (*G*) for α-$^4C_1$ conformations of D-allopyranose[a]

	α-*Anomer*[d]					
	gg(*g*+)-*r*	*gt*(*g*−)-*r*	*tg*(*g*+)-*r*	*gg*(*g*+)-*c*	*gt*(*g*−)-*c*	*tg*(*g*−)-*c*
E	−431352.864	−431352.922	−431351.533	−431352.610	−431351.297	−431353.257
Δ*E*	0.393	0.335	1.724	0.647	1.960	0.000
ZPVE	124.276	124.273	124.498	123.999	123.987	124.454
E + ZPVE	−431228.588	−431228.649	−431227.035	−431228.611	−431227.310	−431228.803
Δ(*E* + ZPVE)	0.600	0.539	2.153	0.577	1.878	0.385
H	132.379	132.403	132.501	132.335	132.273	132.511
S (cal/mol K)	104.925	105.174	104.249	107.250	106.562	104.696
$\Delta(\Delta G^0_{298})$[b]	0.924	0.816	2.578	0.441	1.897	0.732
Hydrogen bonds[c]						
O5···H–O1	2.605	2.602				
H–O1···H–O2			2.238	2.557	2.550	2.588
H–O2···H–O3			2.594			
H–O3···H–O2	2.444	2.451		2.530	2.535	2.512
H–O3···H–O4	2.207	2.222	2.267			
H–O4···H–O3				2.296	2.267	2.238
H–O4···H–O6			2.118			
H–O6···H–O4						2.014
O5···H–O6	2.396	2.431		2.476	2.343	
Bond lengths						
O1–C1	1.426	1.425	1.413	1.401	1.400	1.401
O5–C1	1.408	1.409	1.412	1.428	1.429	1.431
O5–C5	1.449	1.449	1.435	1.434	1.434	1.425
C1–C2	1.538	1.538	1.542	1.543	1.543	1.543
Bond angles						
C1–O5–C5	115.9	115.5	116.0	115.6	115.9	115.1
O1–C1–O5	111.8	112.1	114.0	113.2	113.4	113.1
O1–C1–C2	107.6	107.5	111.0	112.8	113.0	112.9
O5–C1–C2	111.2	110.7	110.4	108.8	108.5	108.7
O2–C2–C1	112.2	112.4	111.5	112.6	112.6	112.6
O5–C5–C6	105.5	105.8	106.6	105.9	105.1	105.7
C1–C2–C3	110.4	110.4	111.0	110.4	110.4	110.4
O5–C5–C4	111.4	110.7	109.2	109.8	109.9	110.6
Dihedral angles						
C5–O5–C1–C2	−57.8	−59.2	−59.3	−61.1	−61.1	−61.6
O5–C1–C2–C3	55.7	55.4	52.4	56.0	56.0	56.6
C1-C2-C3-C4	−52.7	−52.2	−50.4	−53.4	−53.8	−53.3
O5–C5–C6–O6	−58.2	61.9	168.9	−63.0	61.7	179.9
C5–C6–O6–H	59.6	−59.2	52.5	61.5	−50.4	−90.5

[a] All energies in kcal/mol unless otherwise noted. All bond lengths are in Å and bond angles and dihedral angles are in degrees.
[b] $\Delta G^0_{298} = E + (H - TS) + RT$.
[c] The distance for the hydrogen bond cutoff was selected to be <2.6 Å.
[d] Hydroxyl orientations are shown in a condensed form. The full description for the hydroxyl orientations can be found in Tables 2 and 3.

Table 5. Geometry optimized B3LYP/6-311++G** energies (E), harmonic zero point vibrational energies (ZPVE), enthalpies (H), entropies (S), free energies (G), and X-ray diffraction for β-$^4C_1$ conformations of D-allopyranose[a]

	β-*Anomer*[a]						
	gg(*g*+)-*r*	*gt*(*g*−)-*r*	*tg*(*g*+)-*r*	*gg*(*g*+)-*c*	*gt*(*g*−)-*c*	*tg*(*t*)-*c*	*X-ray*[b]
E	−431353.004	−431352.963	−431352.769	−431349.931	−431348.745	−431350.592	
ΔE	0.253	0.294	0.488	3.326	4.512	2.665	
ZPVE	123.816	123.780	124.005	123.575	123.490	123.918	
E + ZPVE	−431229.188	−431229.183	−431228.764	−431226.356	−431225.255	−431226.674	
$\Delta(E$ + ZPVE)	0.000	0.005	0.424	2.832	3.933	2.514	
H	132.087	132.091	132.185	132.006	131.940	132.120	
S (cal/mol K)	106.359	106.728	105.560	107.979	107.919	105.845	
$\Delta(\Delta G^0_{298})$[a]	0.065	0.000	0.636	2.574	3.712	2.663	
Hydrogen bonds[a]							
O5···H–O1	2.518	2.540	2.497				
H–O2···H–O1				2.412	2.416	2.394	
H–O1···H–O2	2.467	2.468	2.479				
H–O2···H–O3	2.311	2.294	2.289				
H–O3···H–O2				2.211	2.208	2.210	
H–O3···H–O4	2.169	2.183	2.191				
H–O4···H–O3				2.302	2.271	2.201	
H–O4···H–O6			2.090				
H–O6···H–O4						1.958	
O5···H–O6	2.367	2.421		2.480	2.342		
Bond lengths							
O1–C1	1.399	1.399	1.398	1.399	1.399	1.398	1.386
O5–C1	1.418	1.419	1.419	1.414	1.415	1.416	1.432
O5–C5	1.441	1.442	1.435	1.432	1.432	1.424	1.447
C1–C2	1.527	1.527	1.528	1.536	1.536	1.535	1.528
Bond angles							
C1–O5–C5	113.7	112.7	112.4	112.7	112.6	112.3	112.3
O1–C1–O5	108.9	109.2	109.1	105.8	105.9	105.9	107.0
O1–C1–C2	107.2	107.1	107.0	111.4	111.6	111.6	114.1
O5–C1–C2	109.8	109.4	109.9	109.6	109.0	109.2	108.3
O2–C2–C1	111.8	111.9	111.9	110.5	110.7	110.5	112.3
O5–C5–C6	105.9	106.3	107.2	106.2	105.5	105.1	108.5
C1–C2–C3	110.4	110.5	110.7	110.8	110.7	110.6	108.2
O5–C5–C4	110.2	109.5	108.6	109.0	108.9	109.9	107.8
Dihedral angles							
C5–O5–C1–C2	−63.4	−65.2	−65.3	−64.9	−66.1	−65.9	−65.1
O5–C1–C2–C3	57.3	57.1	56.1	55.9	56.6	57.2	61.6
C1–C2–C3–C4	−51.0	−50.0	−49.0	−49.0	−49.0	−49.0	−58.0
O5–C5–C6–O6	−57.0	61.6	169.1	−62.9	60.2	−178.4	−75.3
C5–C6–O6–H	57.0	−57.6	50.9	61.5	−52.5	177.1	

[a] See legends in Table 4.
[b] The X-ray diffraction data were taken from Ref. 17.

~0.2 kcal/mol difference in energy favoring glucose over allose is within the error limits expected from these calculations. When the energy is corrected for ZPVE the energy difference becomes ~0.85 kcal/mol, with glucose remaining favored over allose. Thus, epimerization at the C-3 position results in an increase in overall electronic and free energy relative to the lowest energy glucose structure, α-*gt*(*g*−)-$^4C_1$-*r*. A similar destabilization was observed in the mannose study[24] in which epimerization is at the 2-position. Overall, the energetic sequence of the epimers of D-glucopyranose is galactose < glucose < allose < mannose with a B3LYP/6-311++G** energy ranging from −431354.03 kcal/mol for galactose to −431352.62 kcal/mol for mannose.

It is also of interest to examine the energy difference between the lowest energy α- and β-anomers. The energy difference is ~0.2 kcal/mol, giving preference to the α-anomer. When the energy is corrected for the ZPVE, the preference changes to the β-anomer with an energy difference of ~0.4 kcal/mol. The energy difference is small when compared to that found in glucose, mannose, and galactose. Examination of the exocyclic hydroxyl group orientations shows that the '*c*' orientation is favored in the α-anomer case, whereas the '*r*' orientation is favored in the β-anomer with a free-energy difference of ~1 kcal/mol.

A comparison of the X-ray[17] bond distances with the calculated values (see Table 5) for β-$^4C_1$ shows that the

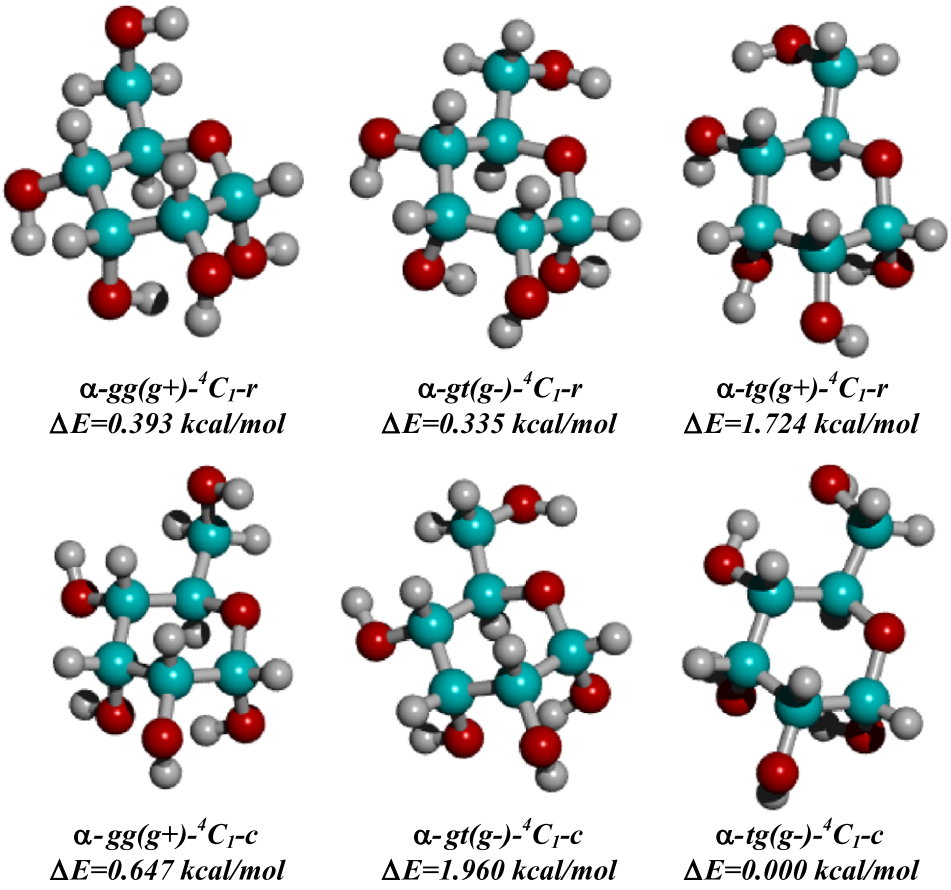

Figure 1. B3LYP/6-311++G** geometry optimized α-D-allopyranose structures in the $^4C_1$ conformation from Table 4.

carbon–carbon ring bond distances are lower by ~0.02 Å relative to the X-ray diffraction data. The experimental bond angles C1–O5–C5, O1–C1–O5, and O5–C1–C2 are reproduced well by the calculations, being within ~2° or better. On the other hand, the bond angle O1–C1–C2 is smaller by ~7° relative to the experimental value of 114°. The above differences between the calculated and experimental bond angles may be attributed to distortion of the structure of β-D-allose in the crystal lattice.

3.3. $^4C_1$ Chair: orientation of exocyclic hydroxyls and hydroxylmethyl group

As mentioned in the previous papers,[23–25] the orientations of the hydroxyl groups and their synergistic energies are crucial factors in relating geometry to energy for the $^4C_1$ conformations. For the α- and β-anomers of $^4C_1$ allose, both '*r*' and '*c*' conformations contain a chain of H–O4···H–O3···H–O2···H–O1 intramolecular interactions (see Tables 4 and 5 and Figs. 1 and 2) with hydrogen-bond distances starting from ~2.1 Å. The *tg* conformers show an additional intramolecular interaction between H–O4···H–O6 in '*c*' and H–O6–H–O4 in '*r*' that exhibit relatively short hydrogen-bond distances of ~2.1–2.0 Å, respectively. In comparison, the *gg* and *gt* conformers show an additional interaction formed between O5···H–O6 with an average hydrogen-bond distance of ~2.4 Å. The formation of the short hydrogen-bond interaction in the α-*tg* and β-*tg* conformers lowered the overall electronic energies compared to the *gg* and *gt* conformers. At this point, it should be mentioned that the discussion refers to the optimum orientation of the H–O6 hydroxyl group either to the ring oxygen O5, or to the H–O4 group. The energetically preferred H–O6 orientation is (*g*+) for the *gg* conformer, (*g*−) for the *gt*, and (*g*−) for the *tg* conformer. For example, the α-*gg*(*g*+)-$^4C_1$-*r* conformer (see Table 2), in which the H–O6 points toward the ring oxygen O5, has a relative energy of ~0.4 kcal/mol whereas the α-*gg*(*g*−)-$^4C_1$-*r* has a relative energy of ~2.6 kcal/mol. The energy difference reflects in part breaking the H–O6···O5 hydrogen bond going from the (*g*+) to the (*g*−) conformation. Thus, care should be taken in defining specific hydroxymethyl conformations.

The lowest energy conformation of allopyranose in this investigation, the α-*tg*(*g*−)-$^4C_1$-*c*, possesses an extensive network of hydrogen bonding, pointing in the clockwise direction around the ring. A similar network of hydrogen bonding is observed for the α-*gg*-*r*

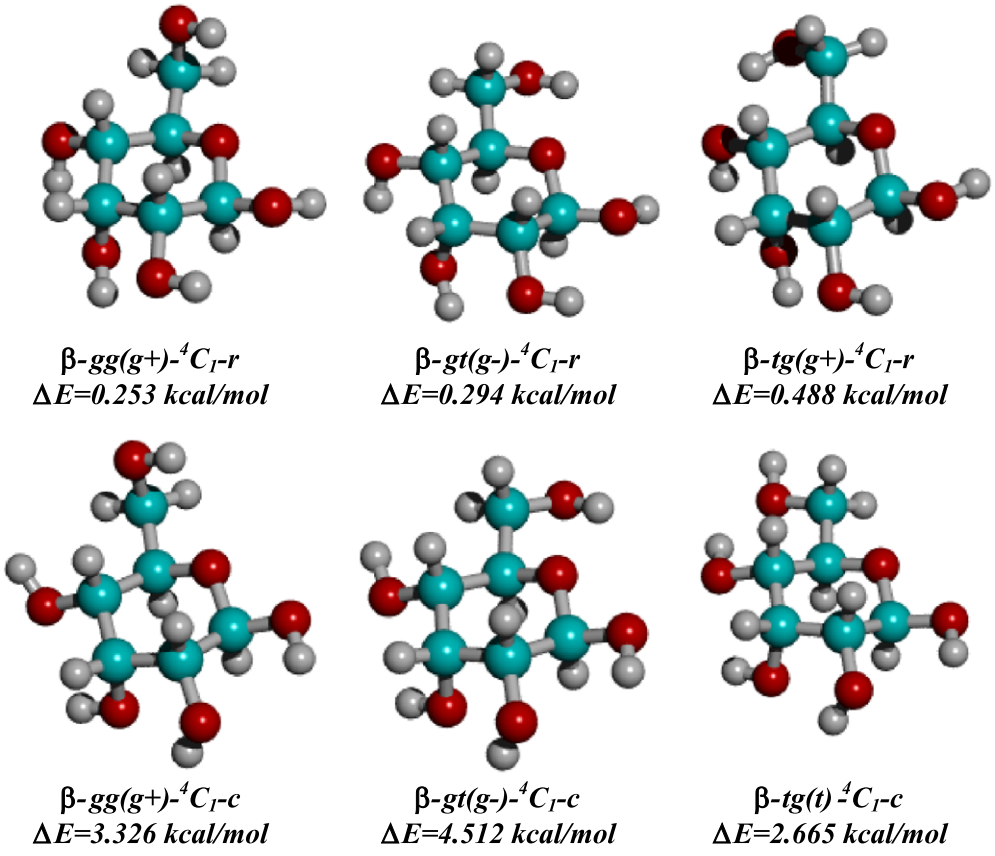

Figure 2. B3LYP/6-311++G** geometry optimized β-D-allopyranose structures in the $^4C_1$ conformation from Table 5.

and α-*gt*-*r* conformers, respectively. The α-*tg*-*r* conformation has the energetic advantage of a shorter H–O6···H–O4 interaction compared to the longer H–O6···O5 interaction (see Table 4) found in *gg* and *gt*, respectively. The picture is reversed in the β-anomer. The energy advantage is given to the counter clockwise '*r*' conformation (see Table 5 and Fig. 2). The energy difference of ~1 kcal/mol can be attributed to the additional H–O1···O5 interaction present in the '*r*' conformation, which is not present in the '*c*' conformation.

In the α-anomers special H–O3···H–O1 and H–O1···H–O3 interactions are observed (see Fig. 1). This type of interaction occurs in the α-$^4C_1$ conformers of allopyranose because of the axial C-1 and C-3 hydroxyl groups. Interactions of axial excocyclic hydroxyls across one ring carbon can be found when there are two non-neighboring exocyclic hydroxyl groups as in other rare sugar epimers of D-glucopyranose.[42] This interaction is not present in the β-$^4C_1$ conformers.

3.4. $^4C_1$ Chair: anomeric influence

The relative energy differences of all examined $^4C_1$ conformations are listed in Table 2 and selected molecular geometries can be found in Tables 4 and 5. The thirty-two calculated α- and β-$^4C_1$ conformations of allopyranose fall within ~12 kcal/mol of each other. The lowest energy α- and β-anomers of the *c* form differ by ~3 kcal/mol, while the '*r*' forms differ by less than ~0.2 kcal/mol. The anomeric ratio of 41:59, as calculated from the free energy, predominately favors the β form since β-*gg*-*r*, β-*gt*-*r*, and β-*tg*-*r* are all of relatively low energy. This is surprising because α-anomers of both '*r*' and '*c*' also contain low relative energies with ΔE of ~0.4 kcal/mol, and the α-*tg*(*g*−) conformer is overall lowest in energy. The difference originates in part from an entropic effect, that is, the average entropy of the β-conformers is ~106.2 cal/mol K and for the α-conformers ~104.9 cal/mol K. Overall, this entropic difference results in an average free energy advantage of ~0.5 kcal/mol for the β-conformers.

There is an anomeric influence on the C1–O5–C5 bond angle. The α-anomers have an average C1–O5–C5 bond angle of ~115.5°, while the β-anomers have an average C1–O5–C5 bond angle of ~113.2°. This result is in line with the results found for glucose, mannose, and galactose. The O1–C1–O5 bond angle shows a small dependency on the '*r*' or '*c*' conformation as the α-anomers in the '*c*' form have an average ~112.4° bond angle, while in the '*r*' form an average bond angle of ~112.8° is found. In the β-anomers, the '*r*' and '*c*' conformational dependence is more pronounced, with

an average O1–C1–O5 bond angle of ~107.7° in the '*c*' form compared to ~108.9° in the '*r*' form.

The ring bond length difference is similar for O5–C1 and O5–C5 in the α- and β-anomers in their '*c*' and '*r*' conformations. Both ring bond lengths show a dependence on the '*c*' and '*r*' conformation. The O5–C1 bond distance shortens from 1.425 to 1.406 Å for the α-anomer and for the β-anomer from 1.428 to 1.415 Å going from the '*c*' to the '*r*' conformation. Thus, the C5–O5 gets longer going from the '*c*' to the '*r*' conformers, the average C5–O5 bond distance changes from 1.430 to 1.444 Å and 1.427 to 1.438 Å for the α- and β-anomer, respectively.

3.5. $^1C_4$ Chair

Changing from the $^4C_1$ conformation to the $^1C_4$ conformation exchanges the positions of the axial and equatorial substituents. The effect of this inversion on allose is to create more disordered hydroxyl interactions where many of the $^1C_4$ conformers have mixed '*r*' and '*c*' hydroxyl orientations (see Table 2). Selected calculations for the vacuum $^1C_4$ conformations of α- and β-D-allopyranose rotamers are presented in Tables 6 and 7 (see also Figs. 3 and 4), respectively. The $^1C_4$ conformations are energetically higher than the $^4C_1$ (ring inversion to the $^1C_4$ form places the hydroxymethyl in the unfavored axial position) with the lowest energy $^1C_4$ being β-*gg*(*g*+)-$^1C_4$-*c*, ~2.6 kcal/mol above lowest $^4C_1$ conformation. Overall, the electronic and relative free energies of the $^1C_4$ conformations are ~3–10 kcal/mol higher than the lowest electronic and relative free energy $^4C_1$ conformations of allopyranose.

For both the α- and β-anomers, the *gg* conformer is preferred. The *gt* rotamer is preferred over the *tg* rotamer in the α-anomer, whereas for the β-anomer

Table 6. Geometry optimized B3LYP/6-311++G** energies (*E*), harmonic zero point vibrational energies (ZPVE), enthalpies (*H*), entropies (*S*), free energies (*G*) for α-$^1C_4$ conformations of D-allopyranose[a]

	α-Anomer[a]					
	gg(t)-r	*gt*(g−)-*r*	*tg*(g+)-*r*	*gg(t)-c*	*gt*(g−)-*c*	*tg*(g+)-*c*
E	−431348.982	−431348.494	−431346.521	−431348.904	−431349.055	−431346.166
Δ*E*	4.275	4.763	6.736	4.353	4.202	7.091
ZPVE	123.894	123.905	123.759	124.081	124.266	123.957
E + ZPVE	−431225.088	−431224.589	−431222.762	−431224.823	−431224.789	−431222.209
Δ(*E* + ZPVE)	4.100	4.599	6.426	4.365	4.399	6.979
H	132.128	132.113	132.066	132.248	132.353	132.246
S (cal/mol K)	105.517	105.679	106.518	105.191	104.974	106.686
$\Delta(\Delta G^0_{298})$[a]	4.379	4.804	6.480	4.674	4.693	6.965
Hydrogen bonds[a]						
O5···H–O1	2.330	2.330	2.309	2.535	2.531	2.533
H–O2···H–O1				2.227	2.257	2.241
H–O1···H–O2	2.207	2.233	2.229			
H–O3···H–O2				2.553	2.592	2.577
H–O4···H–O3	2.357	2.353	2.356	2.153	2.165	2.165
O5···H–O6		2.335			2.311	
Bond lengths						
O1–C1	1.406	1.403	1.403	1.386	1.384	1.385
O5–C1	1.424	1.422	1.418	1.436	1.434	1.430
O5–C5	1.439	1.450	1.442	1.430	1.440	1.434
C1–C2	1.531	1.532	1.533	1.534	1.534	1.536
Bond angles						
C1–O5–C5	117.0	116.4	116.4	116.7	116.1	116.1
O1–C1–O5	106.6	107.1	107.0	107.6	107.8	108.1
O1–C1–C2	106.9	107.0	107.2	111.8	112.2	111.9
O5–C1–C2	112.0	112.1	112.0	110.2	110.4	110.4
O2–C2–C1	110.1	110.2	110.1	106.4	106.3	106.2
O5–C5–C6	112.6	110.3	111.0	113.4	110.7	111.6
C1–C2–C3	109.5	109.4	109.2	111.8	111.4	111.4
O5–C5–C4	112.0	112.1	111.3	111.5	111.6	111.0
Dihedral angles						
C5–O5–C1–C2	55.2	55.1	56.5	57.3	57.5	58.3
O5–C1–C2–C3	−56.2	−56.0	−55.9	−53.6	−54.0	−53.3
C1–C2–C3–C4	55.0	55.2	54.6	50.6	51.2	50.3
O5–C5–C6–O6	−71.5	55.4	161.2	−74.7	54.0	162.6
C5–C6–O6–H	−179.6	−41.5	78.2	176.2	−40.8	84.6

[a] See legends in Table 4.

Table 7. Geometry optimized B3LYP/6-311++G** energies (E), harmonic zero point vibrational energies (ZPVE), enthalpies (H), entropies (S), free energies (G) for β-$^1C_4$ chair conformations of D-allopyranose[a]

	β-*Anomer*[a]					
	gg(*g*+)-*r*	*gt*(*g*+)-*r*	*tg*(*g*−)-*r*	*gg*(*g*+)-*c*	*gt*(*g*−)-*c*	*tg*(*t*)-*c*
E	−431348.612	−431347.394	−431348.550	−431350.656	−431348.354	−431347.460
ΔE	4.645	5.863	4.707	2.601	4.903	5.797
ZPVE	124.271	123.964	124.202	124.701	124.155	123.776
E + ZPVE	−431224.341	−431223.430	−431224.348	−431225.955	−431224.199	−431223.684
$\Delta(E$ + ZPVE)	4.847	5.758	4.840	3.233	4.989	5.504
H	132.386	132.182	132.360	132.568	132.340	132.176
S (cal/mol K)	104.784	105.309	105.302	102.989	105.764	107.026
$\Delta(\Delta G^0_{298})$[a]	5.225	6.083	5.107	3.898	5.145	5.499
Hydrogen bonds[a]						
O5···H–O1	2.627	2.372	2.575	2.622	2.612	2.579
H–O2···H–O3		2.594	2.228			2.470
H–O3···H–O2				2.375	2.519	
H–O3···H–O4			2.438			
H–O4···H–O3	2.332	2.374		2.155	2.170	2.529
O5···H–O6					2.318	
Bond lengths						
O1–C1	1.432	1.409	1.417	1.431	1.415	1.418
O5–C1	1.399	1.413	1.413	1.403	1.416	1.416
O5–C5	1.455	1.437	1.440	1.449	1.450	1.435
C1–C2	1.539	1.538	1.533	1.532	1.530	1.536
Bond angles						
C1–O5–C5	119.1	117.1	117.8	118.8	118.6	117.8
O1–C1–O5	112.8	113.0	112.7	112.4	113.0	112.2
O1–C1–C2	107.5	107.2	106.8	107.5	106.2	107.2
O5–C1–C2	113.4	111.8	112.8	113.8	113.2	113.1
O2–C2–C1	108.9	110.2	111.2	105.7	106.7	111.0
O5–C5–C6	112.8	112.9	112.2	113.7	111.1	112.6
C1–C2–C3	111.1	110.0	110.7	112.6	111.3	110.0
O5–C5–C4	112.2	111.7	112.7	111.5	112.6	112.3
Dihedral angles						
C5–O5–C1–C2	48.8	55.3	52.0	49.0	49.3	51.1
O5–C1–C2–C3	−50.5	−54.0	−52.4	−46.6	−50.7	−52.1
C1–C2–C3–C4	52.7	53.4	52.0	47.8	52.3	53.9
O5–C5–C6–O6	−79.6	30.9	165.0	−79.7	53.9	161.8
C5–C6–O6–H	59.2	51.2	−69.3	61.3	−40.1	174.0

[a] See legends in Table 4.

the reverse is observed. The α-forms of the $^1C_4$ conformations have an average ~2.40 Å O5···H–O1 interaction, whereas in the β-anomers this interaction is weaker, ~2.55 Å. Further, the α-forms of the $^1C_4$ conformations have an ~2.40 Å H–O2···H–O1 interaction. However, this is not found in the β-forms. Comparing the '*c*' and '*r*' conformations of the α- and β-anomers, no clear preference can be given to either form, as was possible for the $^4C_1$ conformers.

The $^1C_4$ conformations exhibit an anomeric influence on bond angle with the C5–O5–C1 average bond angle of ~116.5° for the α-anomers and ~118.5° for the β-anomers.

3.6. Boat forms

Classic boat conformations ($^{3,O}B$, $B_{3,O}$, $^{1,4}B$, $B_{1,4}$, $^{2,5}B$, and $B_{2,5}$) with different hydroxyl orientations were geometry optimized and the energies and geometries of the structures are shown in Tables 8 and 9 (see also Figs. 5 and 6). Similarly to the mannose study, many of the boat forms were not stable and went through transitions to skew forms (see Table 3) during optimization. Of the investigated conformations that retain boat forms, the α-*tg*-$B_{2,5}$-*c* conformer is the most stable.

In case of the $^{1,4}B$ and $B_{1,4}$ forms two stable forms were found: α-*gg*-$^{1,4}B$-*c* and β-*gg*-$B_{1,4}$-*r*. These boat forms are >2 kcal/mol energetically above the lowest *gg*-$^{3,O}B$-*c* and more than ~8 kcal/mol above the lowest energy $^4C_1$ form. The $^{1,4}B$ and $B_{1,4}$ conformations are stabilized by short H–O3···H–O2 and H–O2···H–O3 hydrogen bonds of 1.93 and 1.92 Å, respectively.

The last set of boats investigated were the $^{2,5}B$ and $B_{2,5}$ forms. No stable $^{2,5}B$ conformer was found. All the $^{2,5}B$ forms examined transitioned upon unrestricted optimization to $^OS_2$ skew structures for the α-conformers

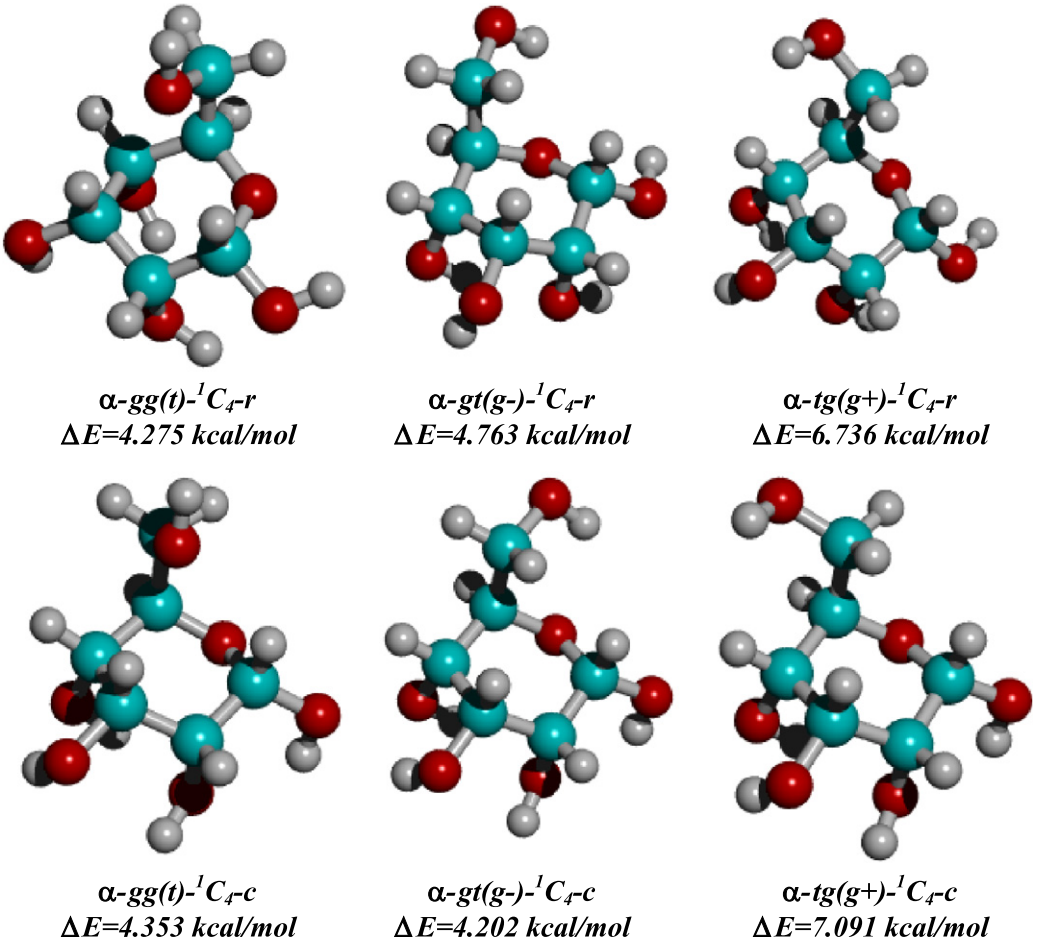

Figure 3. B3LYP/6-311++G** geometry optimized α-D-allopyranose structures in the $^1C_4$ conformation from Table 6.

and $^1S_3$ skews for the β-conformers. The only stable $B_{2,5}$ conformer that did not undergo transitions to other conformations is presented in Figure 5. It is of interest to mention that this conformer has two short interactions of ~1.95 Å for H–O2···H–O3 and H–O3···H–O4, which makes it energetically similar to the $^{3,O}B$ forms.

Generally, the electronic and relative free energies of the boat conformations are ~6–9 kcal/mol higher than the lowest electronic and relative free energy $^4C_1$ conformations of D-allopyranose.

3.7. Skew forms

The stable skew conformers are shown in Tables 10 and 11 (see also Figs. 7 and 8). Most of the skew forms were the result of optimization of boat conformers, for example, with β-$B_{2,5}$ going to β-$^1S_5$ and β-$^{3,O}B$ going to β-$^3S_1$ upon minimization. The skew conformers are of higher energy than the $^4C_1$ conformations with relative energies ranging from ~3 to 10 kcal/mol above the lowest energy $^4C_1$ conformation. When comparing to the α-$^1C_4$, the α-*gg*-$^OS_2$ and α-*gt*-$^OS_2$ conformers are ~0.7 kcal lower than the lowest energy α-$^1C_4$ conformation. The additional stability can be explained by the relative short H–O4···H–O2 interaction of ~2.05 Å, whereas the same interaction for the $^1C_4$ is ~2.15 Å.

4. Discussion

Results from this study of allose conformers can be compared with similar calculations on energetically stable forms of glucose,[23] mannose,[24] and galactose[25] studied at the same level of theory. It is of interest that the electronic energy of the allose conformation, α-*tg*-$^4C_1$-*c*, is only slightly higher that of the lowest energy glucose conformation. This is of course a result of a selective network of hydrogen bonding, especially the axial pairings of H–O3···H–O1 in the α-$^4C_1$-confomers, interactions, which are not in competition with water during these calculations, and thus would not be experimentally functional in solution. Generally speaking, from an energetic point of view, exchanging an equatorial

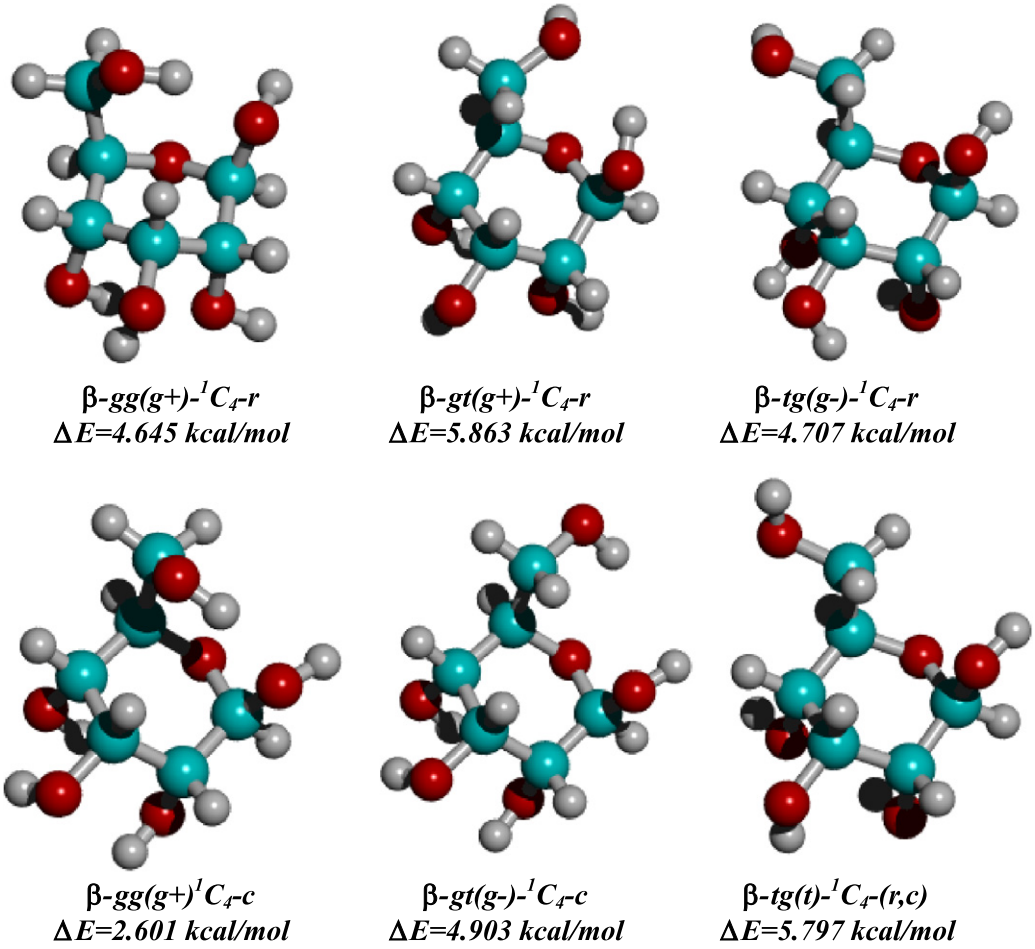

Figure 4. B3LYP/6-311++G** geometry optimized β-D-allopyranose structures in the $^1C_4$ conformation from Table 7.

substituent for an axial one is not preferred and increases the molecular enthalpy. This classical argument only holds when one cannot compensate for this increase in energy through the energy lowering effects of hydrogen bonding, as found in this and previous DFT studies of D-glucopyranose[23–25] epimers.

Considering the α-$^4C_1$ conformations, the comparison between relative energy and relative free energy profiles showed that although the α-anomer is favored from Δ*E* values, using Δ(Δ*G*) values shifts the preference to the β-anomer. One of the β-*gt* conformations has the lowest relative free energy, followed by a β-*gg* conformer at ~0.1 kcal/mol, and a β-*tg* hydroxymethyl conformer at ~0.6 kcal/mol. Similarly to the β-anomers, all three hydroxylmethyl rotamers for the α-anomer have one or more hydroxyl orientation combinations that are within ~1 kcal/mol in relative free energy. The relative free energy difference between the lowest β-anomer and α-anomer is ~0.4 kcal/mol. Overall, this will favor the β-anomer over the α-anomer. From this one could assume that the β-anomers will be preferred in solution, which appears to be in agreement with experimental NMR data.[11] Since the energetic differences of the *gg*/*gt*/*tg* rotamers for both anomers are similar and the energy difference between the anomers is small, similar α and β population should be expected. The calculated in vacuo anomeric ratio is α/β = 41/59%, whereas NMR studies suggest 15/85%. The difference between these vacuum calculations and the experimental results may be explained when hydration effects[42,43] are included. Comparing the structures of the in vacuo α- and β-$^4C_1$ anomers, one would be led intuitively to the conclusion that the β-anomer can be better hydrated than the α-anomer (see Figs. 1 and 2). In the α-anomers the H–O3 and H–O1 hydroxyl groups are not fully accessible to interact with water, whereas in the β-anomer all hydroxyl groups are readily available to interact with water. To quantify the previous argument, studies of glucose epimers using COSMO,[44,45] a dielectric continuum description for the solvent, were carried out and reported.[42] In that presentation, it was shown that when the COSMO method was applied to the epimers of glucose with only one axial hydroxyl group, other than at the anomeric site, the α/β anomeric ratios moved

Table 8. Geometry optimized B3LYP/6-311++G** energies (*E*), harmonic zero point vibrational energies (ZPVE), enthalpies (*H*), entropies (*S*), free energies (*G*) for α-boat conformations of D-allopyranose[a]

	α-*Anomer*[a]	
	gg(*g*+)-^{1,4}*B*-*c*	*tg*(*g*+)-^{2,5}*B*-*r*
E	−431344.460	−431347.240
Δ*E*	8.797	6.017
ZPVE	123.661	124.208
E + ZPVE	−431220.799	−431223.032
Δ(*E* + ZPVE)	8.389	6.156
H	132.089	132.283
S (cal/mol K)	109.768	106.706
$\Delta(\Delta G^0_{298})$[a]	7.595	5.922
Hydrogen bonds[a]		
O5···H–O1	2.609	2.353
H–O2···H–O1	2.101	
H–O1···H–O2		2.110
H–O2···H–O3		1.953
H–O3···H–O2	1.928	
H–O3···H–O4		1.961
H–O4···H–O3	2.303	
H–O4···H–O6		2.061
O5···H–O6	2.608	
Bond lengths		
O1–C1	1.381	1.418
O5–C1	1.435	1.410
O5–C5	1.437	1.443
Bond angles		
C1–O5–C5	117.1	118.1
O1–C1–O5	107.9	109.6
O1–C1–C2	111.0	105.3
O5–C1–C2	111.4	115.2
O2–C2–C1	109.5	110.4
O5–C5–C6	108.3	106.5
C1–C2–C3	111.8	112.6
O5–C5–C4	112.2	107.1
Dihedral angles		
C5–O5–C1–C2	57.2	1.9
O5–C1–C2–C3	−43.5	−46.1
C1–C2–C3–C4	−11.5	31.9
O5–C5–C6–O6	−62.9	168.8
C5–C6–O6–H	70.4	52.4

[a] See legends in Table 4.

Table 9. Geometry optimized B3LYP/6-311++G** energies (*E*), harmonic zero point vibrational energies (ZPVE), enthalpies (*H*), entropies (*S*), free energies (*G*) for β-boat conformations of D-allopyranose[a]

	β-*Anomer*[a]		
	gg(*g*+)$B_{1,4}$-*r*	*gg*(*g*+)-$B_{3,O}$-*c*	*gg*(*t*)-$B_{3,O}$-*r*
E	−431345.138	−431344.702	−431344.196
Δ*E*	8.119	8.555	9.061
ZPVE	123.710	124.210	124.334
E + ZPVE	−431221.428	−431220.492	−431219.862
Δ(*E* + ZPVE)	7.760	8.696	9.326
H	132.045	132.316	132.375
S (cal/mol K)	108.636	106.723	104.683
$\Delta(\Delta G^0_{298})$[a]	7.210	8.487	9.660
Hydrogen bonds[a]			
O5···H–O1	2.359		2.571
H–O1···H–O2	2.523		
H–O2···H–O3	1.917		
H–O3···H–O2		2.431	
H–O3···H–O4	2.119	2.328	2.209
H–O4···H–O3			
O5···H–O6	2.538		
Bond lengths			
O1–C1	1.402	1.433	1.400
O5–C1	1.418	1.399	1.431
O5–C5	1.446	1.458	1.442
C1–C2	1.531	1.555	1.548
Bond angles			
C1–O5–C5	114.8	119.8	119.1
O1–C1–O5	108.7	108.7	113.4
O1–C1–C2	111.4	112.1	112.4
O5–C1–C2	107.6	113.2	111.5
O2–C2–C1	111.5	110.7	111.2
O5–C5–C6	105.9	112.5	112.6
C1–C2–C3	111.8	110.1	111.0
O5–C5–C4	113.0	112.3	113.1
Dihedral angles			
C5–O5–C1–C2	−69.8	41.4	38.3
O5–C1–C2–C3	53.1	14.0	20.4
C1–C2–C3–C4	1.3	−59.9	−64.8
O5–C5–C6–O6	−63.4	−74.6	−70.4
C5–C6–O6–H	66.6	67.8	−172.0

[a] See legends in Table 4.

closer to the experimental values, relative to the vacuum values. For example, the anomeric α/β ratio for allose became 38/62. However, application of COSMO to the di- and tri-axial group epimers resulted in significantly different anomeric ratios from experimental values.[42,46] There have recently been several successful DFT solvation studies reported that place explicit water molecules around D-glucopyranose epimers[32,33] as well as around the larger cellobiose[35,36] molecule. Further, DFT solvation studies for all the epimers of D-glucopyranose are currently ongoing and the results of this study will be reported elsewhere.

The clockwise '*c*' and counter clockwise '*r*' orientations of the exocyclic hydroxyl groups are favored for some hydroxymethyl orientations but depend upon the hydrogen bonding network available. Special hydrogen bonds across one ring carbon were observed in α-$^4C_1$ conformers (H–O3···H–O1 and H–O1···H–O3 interactions) and α- and β-$^1C_4$ conformers (H–O1···H–O4 and H–O2···H–O4). These types of hydrogen bonds have been observed previously in the chair forms of the rare sugars idose and talose.[42] In addition to the significance of the exocyclic hydroxyl group orientations on the ring geometries and relative energies of allose, it is also important to notice the different orientation of the H–O6 hydroxyl group. In general, the *gg* rotamer prefers a (*g*+) orientation regardless of the '*c*' or '*r*' orientation, whereas for the *gt* and *tg* it is either (*g*+) or (*g*−) depending on the hydrogen network formed by the '*c*'

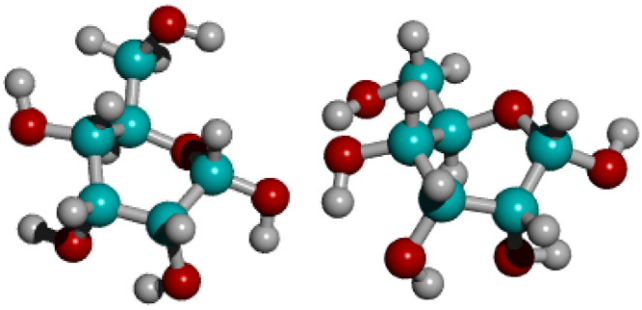

Figure 5. B3LYP/6-311++G** geometry optimized α-D-allopyranose boat conformations from Table 8.

or '*r*' conformation. In most cases, the (*t*) orientation is not preferred except in α-*gg*-$^{1}C_4$ (see Fig. 3) where the (*g*+) and (*g*−) orientations are energetically higher because of the repulsive interaction between the lone pairs of the O6 oxygen atom with C5 or O5, respectively.

The $^{1}C_4$ conformations are all of higher energy than the $^{4}C_1$ with the *gg* conformation being the lowest energy conformer for both α- and β-anomers. All the boat and skew conformers are of relatively high energy with relative energies ranging from ~6 to 9 kcal/mol for the boat forms and ~3.3 to 10 kcal/mol for the skew forms above the lowest energy $^{4}C_1$ conformation. Somewhat surprising was the observation that the α-*gg*-$^{O}S_2$ and α-*gt*-$^{O}S_2$ conformations were only ~3.3 kcal/mol higher in energy than the lowest energy form. These were the only medium energy conformations of a boat or skew form found, with none of the other stable conformers close to this value.

It is sometimes instructive to present information relative to the computational methods used, that is the basis set size and density functionals used for carbohydrate studies in this laboratory, and to clarify some points relative to the epimer calculations. For that reason we describe here an overview of the criteria used to choose the computational methods and their application to carbohydrates. When comparing the two basis sets used herein, the smaller, 6-31+G*, is for most cases adequate (see Fig. 9) giving geometries and relative energies in fairly close agreement with the larger basis set, that is, 6-311++G**. Comparing the relative allose energies (see Fig. 9) that arise from these two basis sets, the ΔE values found are of the order of several tenths of kcal/mol with a slope of 0.94. The maximum outliers deviate by up to ~2 kcal/mol, with ~24% having ΔE values of ~0.5 kcal/mol or greater. Although these data indicate some correspondence between basis sets, it remains that under specific conformational conditions the small basis set prefers hydroxyl configurations that change orientation when re-optimized with the larger basis set. This occurred in 17 of 103 cases, and it is not possible to ascertain when these conformational shifts will take place. It was also found that the differences between the basis sets were sufficient to misplace two minimum energy conformations, one hydroxymethyl conformation, and in some cases completely change the relative energy ordering of conformers. The rotamer changes were observed in several low energy cases as well as high energy structures and therefore cannot be attributed to high energy structures under stress. We do not recommend reporting the small basis set structures since they may be misleading.

When comparing the smaller HF/6-21G* basis sets,[22] there are significant differences in relative energies between our results and theirs, being on average ~2.5 kcal/mol difference between the α-anomers of allose, and ~0.25 kcal/mol difference for the β-anomer. It is possible that the lowest energy α-anomer conformations were not found in the HF study and that could account for the rather large deviations in energy for the α-series. The empirical OPLS-AA potentials[22] derived from the HF structures also show a similar trend, deviating by ~2.3 kcal/mol for the α-anomer

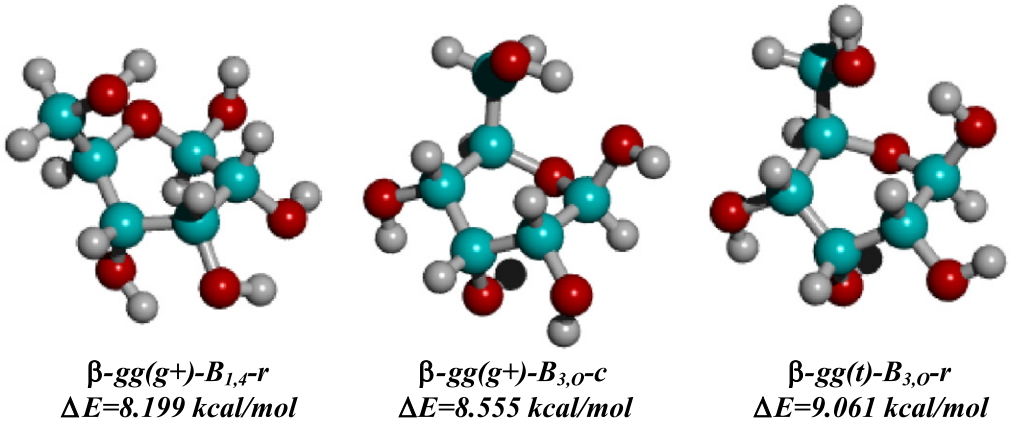

Figure 6. B3LYP/6-311++G** geometry optimized β-D-allopyranose boat conformations from Table 9.

Table 10. Geometry optimized B3LYP/6-311++G** energies (*E*), harmonic zero point vibrational energies (ZPVE), enthalpies (*H*), entropies (*S*), free energies (*G*) for α-skew conformations of D-allopyranose[a]

	α-*Anomer*[a]							
	gg(*t*)-$^1S_3$-*r*	*gt*(*g*−)-$^1S_3$-*r*	*tg*(*g*+)-$^1S_3$-*c*	*gg*(*g*+)-$^OS_2$-(*r*,*c*)	*gt*(*g*−)-$^OS_2$-(*r*,*c*)	*tg*(*t*)-$^OS_2$-*c*	*gg*(*g*+)-$^OS_2$-*c*	*gt*(*g*−)-$^OS_2$-*c*
E	−431345.723	−431345.175	−431343.696	−431349.973	−431349.914	−431348.121	−431347.402	−431347.093
Δ*E*	7.534	8.082	9.561	3.284	3.343	5.136	5.855	6.164
ZPVE	123.691	123.648	124.452	124.329	124.247	123.919	124.098	124.098
E + ZPVE	−431222.032	−431221.527	−431219.244	−431225.644	−431225.667	−431224.202	−431223.304	−431222.995
Δ(*E* + ZPVE)	7.156	7.661	9.944	3.544	3.521	4.986	5.884	6.193
H	132.020	131.954	132.429	132.390	132.347	132.166	132.290	132.241
S (cal/mol K)	107.311	107.715	104.592	104.925	105.215	107.388	106.446	105.931
$\Delta(\Delta G^0_{298})$[a]	6.995	7.357	10.242	3.826	3.756	4.720	5.844	6.258
Hydrogen bonds[a]								
O5···H–O1	2.330	2.326	2.727	2.518	2.525			
H–O2···H–O1			2.008			1.991	1.949	1.959
H–O1···H–O2	2.016	2.031		2.096	2.081			
H–O2···H–O3	1.951	1.955						
H–O3···H–O2			2.068			2.318		
H–O3···H–O4	2.293	2.305						
H–O4···H–O3				2.154	2.163	1.910	2.232	2.237
H–O4···H–O6			2.266					
H–O6···H–O4						2.073	2.431	2.381
O5···H–O6		2.422		2.417	2.447			
Bond lengths								
O1–C1	1.404	1.403	1.374	1.415	1.415	1.396	1.391	1.390
O5–C1	1.415	1.412	1.447	1.413	1.413	1.429	1.433	1.434
O5–C5	1.441	1.454	1.438	1.445	1.445	1.424	1.427	1.427
C1–C2	1.541	1.542	1.558	1.544	1.545	1.547	1.562	1.535
Bond angles								
C1–O5–C5	114.8	114.8	114.0	116.0	115.6	114.8	115.1	115.2
O1–C1–O5	107.3	107.8	108.9	112.0	112.3	112.1	111.9	112.1
O1–C1–C2	107.3	107.3	111.9	106.8	106.7	111.3	110.9	111.1
O5–C1–C2	112.1	112.5	109.3	113.3	113.0	111.9	111.4	111.2
O2–C2–C1	112.0	112.0	110.2	111.7	111.8	107.6	110.4	110.4
O5–C5–C6	110.8	109.2	112.6	105.9	106.2	106.5	106.2	105.9
C1–C2–C3	110.6	110.8	110.2	107.8	107.8	111.8	108.7	108.8
O5–C5–C4	112.6	112.7	110.6	111.0	110.9	109.1	110.5	110.7
Dihedral angles								
C5–O5–C1–C2	65.3	64.2	69.1	−33.9	−35.7	−34.5	−42.7	−42.7
O5–C1–C2–C3	−37.2	−37.4	−26.6	−29.5	−28.2	−27.1	−21.6	−21.6
C1–C2–C3–C4	−22.0	−21.6	−35.7	65.8	65.8	52.6	63.1	63.4
O5–C5–C6–O6	−65.5	59.9	165.8	−59.9	62.3	−173.5	−60.8	63.1
C5–C6–O6–H	−176.3	−49.8	44.8	59.1	−58.5	178.9	60.4	−50.4

[a] See legends in Table 4.

and ~1.1 kcal/mol for the β-anomers. In both anomers, there are differences as to which of the conformers are actually lowest in energy, again a possible result of our finding lower energy α-anomers than those found in their work.[22]

Regarding the B3LYP density functional used throughout our DFT studies, it has been well established in the literature[47] that this DFT with our large basis set results in excellent geometry.[47] The question of the relative energies requires a comparison with other DFT's. Our and other analysis suggests that there are some cases where other DFT methods result in better agreement with higher level studies.[48] It is clear that the energy differences are small and result in an absolute error in energy from the B3LYP density functional of ~1 kcal/mol. However, it is seen most often that relative energies of one molecule are compared within one calculation method, and in this case almost all the DFT methods (PBE[49], B97[50], B97-1[51]) tested by us enjoy similar and rather small deviations. In the case of B3LYP, relative deviations are of the order of ~0.1 kcal/mol or less. In analyzing α/β anomeric energy differences, using the published example of the 2-hydroxytetrahydropyrane, the B3LYP/6-311++G** DFT combination differs by ~0.04 kcal/mol from the CCSD(T) results,[48] although it was clear that removing the diffusion terms could change the relative energies by as much as ~0.4 kcal/mol.

Table 11. Geometry optimized B3LYP/6-311++G** energies (*E*), harmonic zero point vibrational energies (ZPVE), enthalpies (*H*), entropies (*S*), free energies (*G*) for β-skew conformations of D-allopyranose[a]

	β-*Anomer*[a]									
	gg(*g*+)-$^{1}S_{3}$-*c*	*gg*(*g*+)-$^{1}S_{5}$-*c*	*gt*(*g*−)-$^{1}S_{5}$-*r*	*tg*(*g*+)-$^{1}S_{5}$-*r*	*gg*(*g*+)-$^{3}S_{1}$-*r*	*gt*(*g*−)-$^{3}S_{1}$-*r*	*gg*(*g*+)-$^{O}S_{2}$-*c*	*gt*(*g*+)-$^{O}S_{2}$-*r*,*c*	*gg*(*g*+)-$^{2}S_{O}$-*r*	*tg*(*g*−)-$^{2}S_{O}$-*r*
E	−431345.407	−431347.258	−431345.513	−431346.341	−431346.542	−431346.329	−431347.201	−431343.985	−431346.712	−431343.171
Δ*E*	7.850	5.999	7.744	6.916	6.715	6.928	6.056	9.370	6.545	10.086
ZPVE	123.589	123.812	123.758	124.107	123.750	123.613	124.005	123.600	124.114	123.632
E + ZPVE	−431221.818	−431223.446	−431221.755	−431222.234	−431222.792	−431222.716	−431223.196	−431220.385	−431222.598	−431219.539
Δ(*E* + ZPVE)	7.370	5.742	7.433	6.954	6.396	6.472	5.992	8.803	6.590	9.649
H	132.040	132.157	132.102	132.259	132.096	131.994	132.242	131.975	132.293	132.076
S (cal/mol K)	8.451	8.345	8.344	8.152	8.346	8.381	107.634	107.701	8.179	8.444
$\Delta(\Delta G^{0}_{298})$[a]	6.471	5.451	7.145	7.015	5.830	5.979	5.643	8.086	6.711	9.366
Hydrogen bonds[b]										
O5···H–O1		2.540	2.481	2.475	2.523	2.539	2.400	2.487	2.576	2.552
H–O2···H–O3			1.956	1.952	1.918	1.928		2.180	2.533	2.510
H–O3···H–O2	2.056	1.995					2.596			
H–O3···H–O4			1.988	1.992	2.236	2.320			2.148	2.055
H–O4···H–O3	2.507	2.003					2.107			
H–O4···H–O6				2.052						
O5···H–O6		2.548	2.358		2.459	2.297	2.422	2.310		
Bond lengths										
O1–C1	1.439	1.419	1.418	1.419	1.399	1.398	1.395	1.388	1.437	1.422
O5–C1	1.400	1.417	1.404	1.404	1.421	1.421	1.429	1.430	1.398	1.408
O5–C5	1.448	1.444	1.456	1.448	1.444	1.445	1.433	1.437	1.446	1.437
C1–C2	1.554	1.527	1.531	1.532	1.526	1.527	1.540	1.553	1.538	1.535
Bond angles										
C1–O5–C5	119.1	118.0	118.4	118.1	113.6	112.8	113.6	113.8	119.9	118.3
O1–C1–O5	111.1	111.2	112.3	112.3	108.7	109.1	107.4	108.4	111.9	112.4
O1–C1–C2	107.9	106.1	105.5	105.5	107.2	107.5	108.2	114.1	106.0	105.7
O5–C1–C2	115.0	113.3	113.2	113.4	109.2	108.8	112.3	109.4	115.0	114.3
O2–C2–C1	111.0	107.3	110.1	110.1	111.2	111.5	107.6	112.0	111.0	111.0
O5–C5–C6	110.2	106.2	105.8	106.4	105.3	105.5	106.4	105.6	111.3	110.8
C1–C2–C3	112.4	110.5	110.7	110.6	111.2	110.6	110.6	110.5	110.9	110.8
O5–C5–C4	113.1	109.6	110.8	110.3	112.5	112.2	110.7	111.5	113.7	113.5
Dihedral angles										
C5–O5–C1–C2	50.1	22.8	27.4	27.3	−72.3	−74.0	−48.0	−68.0	28.6	25.0
O5-C1–C2–C3	−16.0	−58.0	−58.9	−58.8	43.7	40.2	−14.1	20.7	26.0	32.5
C1–C2–C3–C4	−37.0	30.4	28.8	27.7	13.6	19.0	57.4	40.8	−60.6	−61.1
O5–C5–C6–O6	−79.0	−67.5	59.1	165.5	−61.8	55.1	−60.2	57.5	−70.3	173.7
C5–C6–O6–H	46.3	61.4	−53.8	51.2	62.5	−53.0	58.6	−50.8	67.3	−63.2

[a] See legends in Table 4.

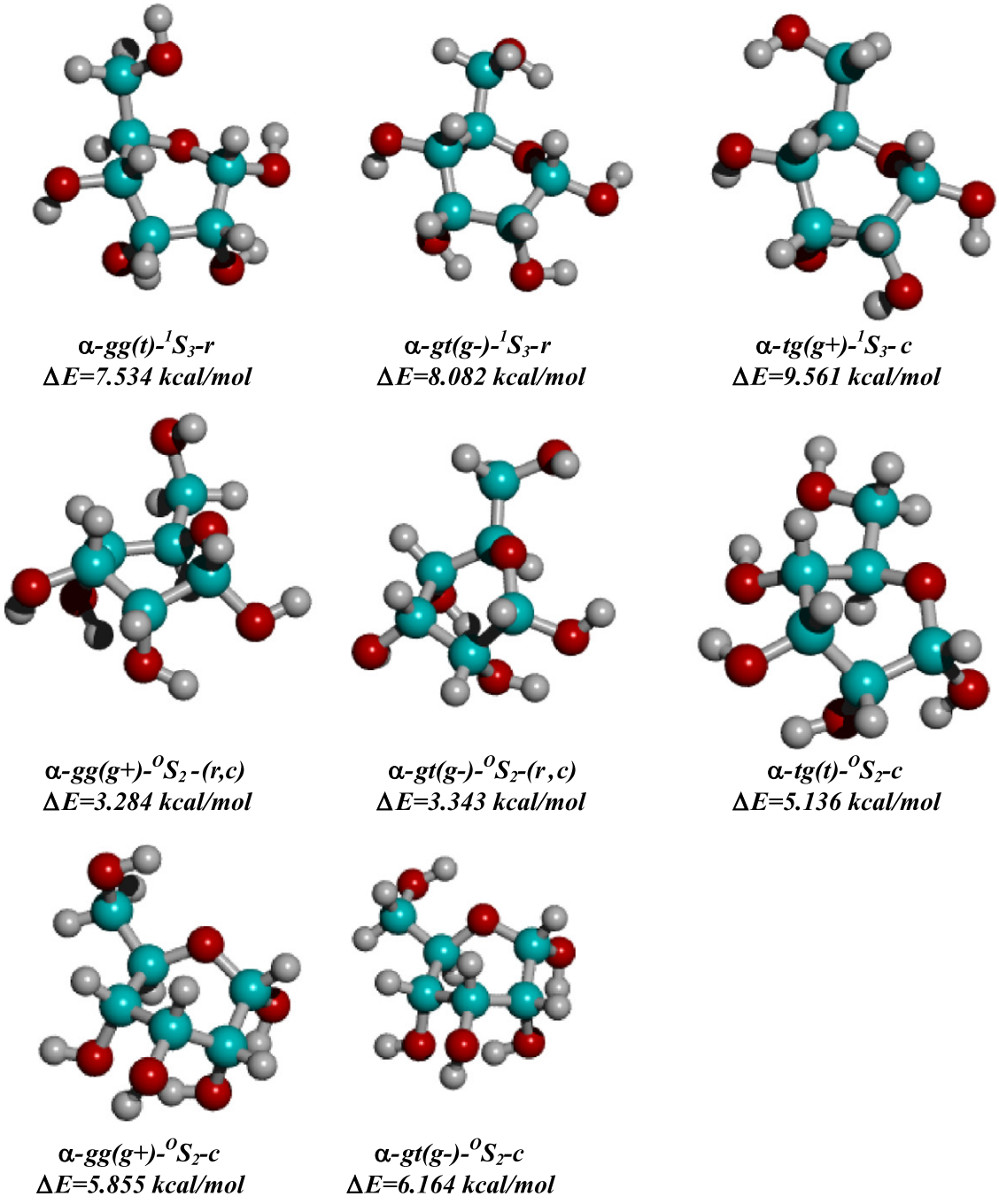

Figure 7. B3LYP/6-311++G** geometry optimized α-D-allopyranose skew conformations from Table 10.

It has also been suggested that our basis set, B3LYP/6-311++G**, is too large[31] and should not be used for carbohydrate studies. When comparing our optimized structures with those obtained from larger and smaller basis sets (see Table 12) the results are not consistent with this premise. From Table 12, it is clear, for all practical purposes that the results are converged within the B3LYP/6-311++G** level of theory. Larger basis sets do not change the α/β energy differences significantly, while smaller basis sets can cause large deviations, even reversing the stability of the anomers. In the study presented in Table 12, we have geometrically optimized the particular structure at each basis set. This is a very different procedure from that of optimizing at a small basis set, and then calculating single point energies for that geometry at a larger basis set and finally comparing the energies.[31] Their approach[31] did not answer the question: 'Can one use a smaller basis set for carbohydrates?'.

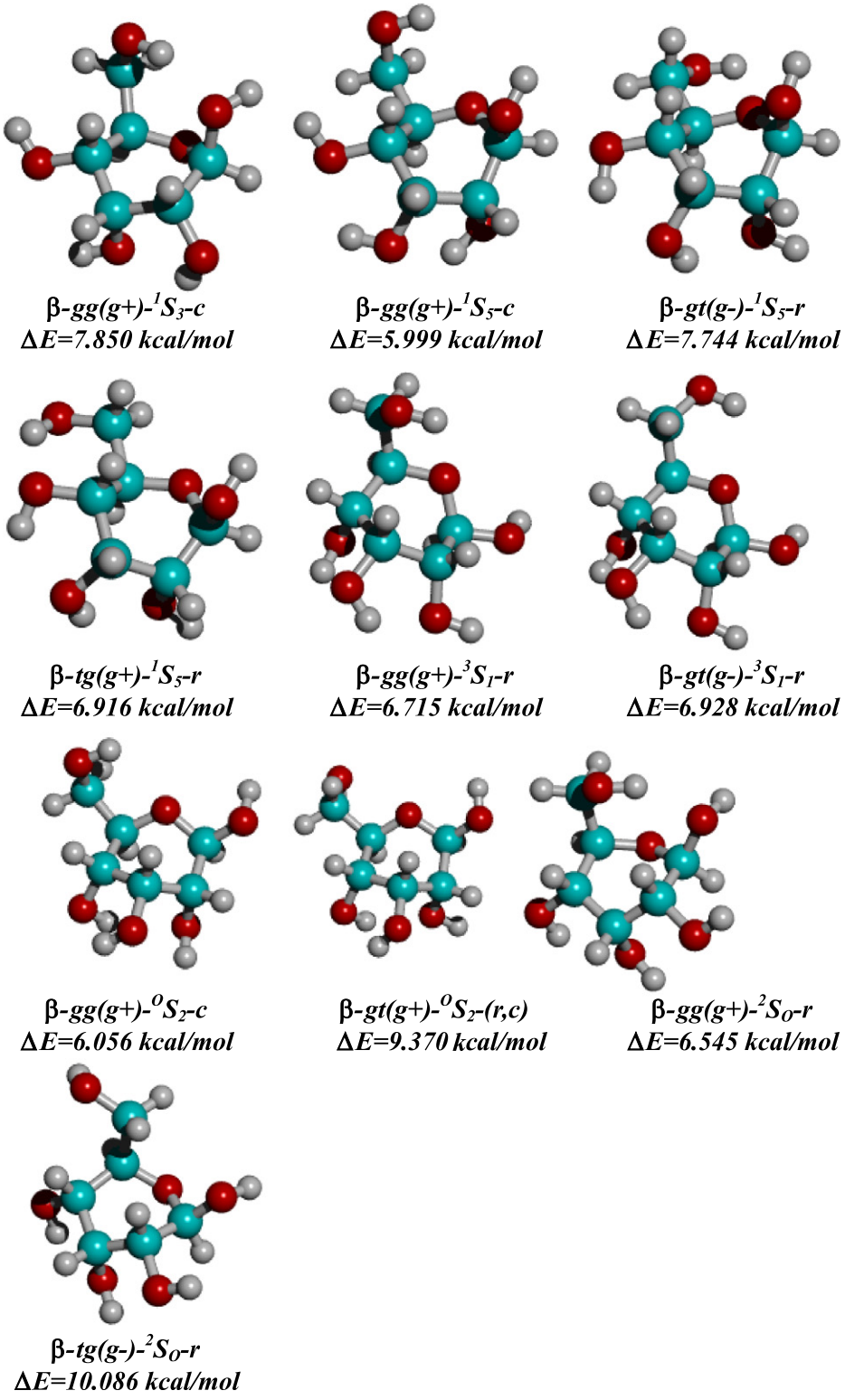

Figure 8. B3LYP/6-311++G** geometry optimized β-D-allopyranose skew conformations from Table 11.

In our study of Pople basis sets larger than 6-311++G**, retaining the B3LYP density functional, we find nearly identical structures and relative energies (see Table 12). Smaller basis sets do not give us small relative terms. Further, the relative free energies resulting from the larger Pople basis sets remain in agreement with those obtained from our study, as do the anomeric populations.

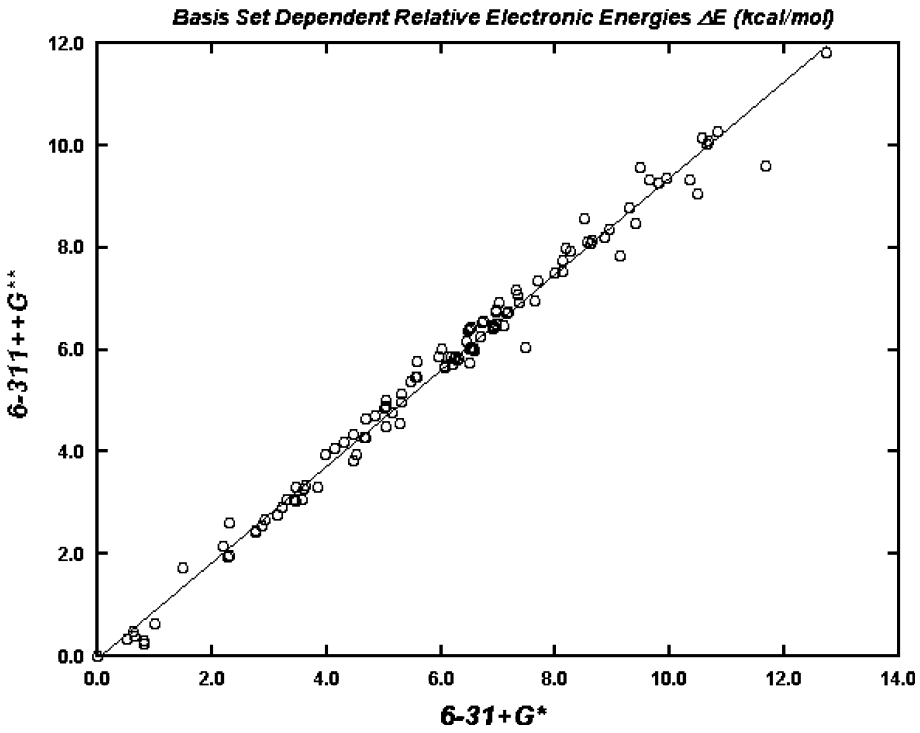

Figure 9. Plot of optimized relative electronic energies ΔE (kcal/mol) of D-allopyranose conformations for B3LYP/6-311++G** versus B3LYP/6-31+G*.

Table 12. Geometry optimized B3LYP relative[a] energies, harmonic zero point vibrational energies, enthalpies, entropies, free energies, and anomeric populations calculated for different Pople basis sets for the lowest α- and β conformer of D-allopyranose

Basis set	Primitive functions	Relative energy (α − β) (kcal/mol)	Relative zero point energy (kcal/mol)	Relative enthalpy (kcal/mol)	Relative entropy (cal/mol K)	Relative free energy (α − β) (kcal/mol)	Anomeric population[b] (%)
α-$^4C_1$-*tg(g−)-c*							
6-31G*	382	−2.347	0.678	0.511	−1.172	−2.058	36.3
6-31+G*	432	−0.558	0.014	−0.009	−0.099	−0.250	54.2
6-31++G**	480	−0.219	0.143	0.135	−0.032	−0.094	55.8
6-311G*	432	−1.395	0.627	0.464	−1.165	−1.435	42.3
6-311++G**	528	0	0	0	0	0	56.7
6-311++G(2d,2p)	624	0.016	0.124	0.158	0.188	0.156	58.2
6-311++G(3d,3p)	720	−0.107	−0.128	−0.078	0.365	0.126	58.0
6-311++G(2df,2pd)	768	0.221	−0.023	0.010	0.200	0.278	59.4
6-311++G(3df,3pd)	864	0.066	−0.014	0.021	0.272	0.449	61.1
β-$^4C_1$-*gg(g+)-r*							
6-31G*	382		0.832	0.561	−1.975		63.7
6-31+G*	432		0.204	0.102	−0.760		45.8
6-31++G**	480		0.213	0.169	−0.336		44.2
6-311G*	432		0.59	0.423	−1.168		57.7
6-311++G**	528		0	0	0		43.3
6-311++G(2d,2p)	624		0.213	0.199	−0.145		41.8
6-311++G(3d,3p)	720		0.014	−0.014	−0.203		42.0
6-311++G(2df,2pd)	768		0.011	0.023	0.053		40.6
6-311++G(3df,3pd)	864		0.225	0.164	−0.535		38.9

[a] Relative with respect to the B3LYP/6-311++G** calculated values.
[b] The anomeric populations were calculated only for the two structures shown in this table.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2006.12.006.

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