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Conformation and Anomer Ratio of D-Glucopyranose in Different Potential Energy Functions

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For low-energy conformers of α- and β-D-glucopyranose, a two-parameter Lennard-Jones function is just as adequate as a three-parameter Buckingham exp-6 function in representing the non-bonded interactions.

When Coulomb interactions based on the monopole approximation are included, it makes essentially no difference whether the anomeric carbon atom is given its proper charge or is treated as any other carbon atom.

These results imply that it is sensible to employ much fewer parameters in consistent potential energy functions than indicated by theoretical considerations.

In the course of the development of a new potential energy function (PEF) to postdict and predict structures, vibrational spectra, dipole moments and thermodynamic properties of several classes of molecules it is of paramount interest to keep down the number of parameters in the PEF.

The present investigation was initiated to answer two questions. (1) In some applications, Coulomb interactions are not necessary. Then non-bonded interactions are usually represented by Buckingham 6-exp functions. Will Lennard-Jones functions, with two rather than three parameters per interaction, give comparable results? (2) When Coulomb terms are necessary, the most sensible approach to initial choice of parameters is to reproduce charges calculated by Mulliken population analysis of *ab initio* results found with reasonably large basis sets. If more than one type of the same atom, say carbon, are present, what are the consequences of neglecting this distinction?

For a test case, D-glucopyranose (Glc) was selected, as rather elaborate calculations on this compound are already available.

The structures of α and β anomers of Glc have been calculated by energy minimisation with full relaxation of all coordinates, using three different PEF's, PEF3,[1] PEF300[2] and PEF400.[3] From calculated free enthalpy differences, equilibrium ratios were calculated. All calculated data fitted well to experimentally observed values, with the single exception of the short anomeric C1–O1 bond.

PEF300 is just a slight correction to PEF3, as the torsional (Pitzer) terms were removed, but PEF400 is a completely different set of functions, incorporating Coulomb interactions into the non-bonding part, and with different sets of bond and angle deformation parameters.

In the present work more conformers are studied than in the earlier papers. They all have the same ring conformation, 4C1, but differ in exocyclic torsions. Altogether six conformers are now minimised in PEF300 and PEF400 and in two variants of these, PEF301 and PEF422.

In PEF301, the Buckingham 6-exp functions for non-bonded interactions of PEF300 are substituted by Lennard-Jones 12-6 functions, with ε and r* fitted to reproduce the minima of the original functions. This is done in order to see whether these two-parameter functions give as good a representation as the three-parameter functions.

In PEF422, the anomeric carbon atom C1 is given a charge parameter different from the other carbon atoms. The change has implications for all atomic charges; but all other parameters are left unchanged. This is done in order to see whether a better fit to results of Mulliken population analysis of *ab initio* calculations[4] with IBMOL-6 would cause significant changes.

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Table 1. Non-bonded functions of PEF301. $E_{n-b} = \varepsilon(r/r^*)^{12} - 2\varepsilon(r/r^*)^6$

	ε/kJ mol^{-1}	r^*/Å
O---O	0.4152	3.260
O---C	0.4153	3.373
O---H	0.2943	3.023
C---C	0.4101	3.498
C---H	0.2817	3.152
H---H	0.1486	2.979

Table 2. Atomic charges.

Parameters	PEF400	PEF422	
O.	−0.400	−0.400	
K.	−0.050	+0.300	
C.	−0.050	+0.050	
H.	+0.125	+0.200	
Assignments	PEF400	PEF422	ab initio[4]
O(KOC)	−0.407	−0.465	−0.422
O(OH)	−0.407	−0.465	−0.531
K[a]	−0.057	+0.235	+0.203
C(CHOH)	−0.057	−0.015	−0.007
C(CH2)	−0.057	−0.015	−0.180
H(O)	+0.393	+0.335	+0.360
H(C)	+0.118	+0.135	+0.185
Dipole moment α	2.24	1.62	2.74
β	3.27	2.41	4.64

[a] K is the anomeric carbon atom C1.

CALCULATIONS

The program. The Consistent Force Field system[5] was used, with later additions for thermodynamics[6] and changes for charge handling.[7]

Potential energy functions. PEF300 is described[2] as a modification to PEF3;[1] it is also listed separately.[8] PEF400 is also available in the literature.[3,7,9] The non-bonded functions of PEF301 are presented in Table 1, and the charge parameters of PEF400 and PEF422 in Table 2, together with atomic charges assigned by the program for PEF400 and PEF422, and calculated by Mulliken population analysis of results from IBMOL-6.[4]

Initial conformations. Two conformers of the α and two of the β anomers as found with PEF400[9,10] were used, the global minima having O6 *gauche* to O5 and *anti* to C4, two others, with O6 *minus-gauche* to O5 and *gauche* to C4. In addition, the global minima of α and β in PEF300[2] were used; they have O6 *gauche* to O5 and *anti* to C4 and differ from the former in the exocyclic torsions around C2−O2, C3−O3 and C4−O4.

Minimisation. 20 steepest-descent plus 10−15 modified Newton iterations sufficed to minimise all conformations which were not already in minimum (2 in PEF300[2] and 4 in PEF400[9,10]).

Thermodynamics. The free enthalpy was calculated at 298K. Statistical summation over translations and rotations was left out, as the calculated equilibrium ratios are compared with values measured in aqueous solution.

Table 3. Conformational details for D-glucopyranose. Angles in degrees, energy terms in kJ mol^{-1}.

	α-Anomer			β-Anomer		
PEF300						
O5−C1−O1	110.7	110.6	110.8	109.1	109.1	108.9
C5−O5−C1	113.4	113.4	113.4	112.5	112.5	112.5
O5−C1−O1−H	60.7	61.0	60.1	52.0	52.0	−64.4
C1−C2−O2−H	−67.8	−67.9	72.9	81.8	81.8	160.6
C2−C3−O3−H	−81.0	−81.1	−159.4	−79.5	−80.0	−159.1
C3−C4−O4−H	81.4	81.8	−62.0	81.2	81.6	−62.4
C4−C5−C6−O6	−173.5	59.4	−179.6	−174.2	59.1	−179.8
O5−C5−C6−O6	65.4	−62.5	59.6	65.1	−62.3	59.7
C5−C6−O6−H	−77.3	75.2	72.6	−77.6	75.0	73.0
E	5.602	6.016	5.410	3.783	4.115	4.127
G	477.021	478.030	476.829	473.995	474.925	474.830
ΔE	1.819	2.233	1.627	0.000	0.332	0.344
ΔG	3.026	4.035	2.834	0.000	0.930	0.835
n_i	0.092	0.061	0.099	0.311	0.214	0.222

Table 3. Continued.

	α-Anomer			β-Anomer		
PEF301						
O5–C1–O1	110.8	110.8	111.0	109.1	109.1	108.9
C5–O5–C1	113.8	113.8	113.8	113.8	113.3	113.2
O5–C1–O1–H	55.3	55.3	54.6	52.6	52.6	−57.4
C1–C2–O2–H	−66.3	−66.6	64.7	70.8	70.7	170.3
C2–C3–O3–H	−70.2	−70.3	−169.9	−69.4	−69.5	−169.6
C3–C4–O4–H	70.5	70.3	−61.9	70.7	70.5	−62.3
C4–C5–C6–O6	−172.2	58.7	178.8	−172.9	58.3	178.6
O5–C5–C6–O6	66.6	−63.3	58.0	66.3	−63.2	58.1
C5–C6–O6–H	−68.3	67.2	66.3	−68.6	67.1	66.5
E	13.006	13.512	12.595	11.769	12.160	11.818
G	495.338	496.612	494.945	493.233	494.378	493.628
ΔE	1.237	1.743	0.826	0.000	0.391	0.049
ΔG	2.105	3.379	1.712	0.000	1.145	0.395
n_i	0.117	0.070	0.137	0.273	0.172	0.233
PEF400						
O5–C1–O1	111.6	111.5	112.0	109.0	109.0	109.4
C5–O5–C1	113.5	113.6	113.6	113.7	113.8	113.7
O5–C1–O1–H	45.2	45.1	43.9	38.3	37.8	−33.0
C1–C2–O2–H	−54.1	−54.2	46.9	47.6	47.6	−178.9
C2–C3–O3–H	−48.6	−48.5	172.4	−52.4	−52.4	168.8
C3–C4–O4–H	52.9	53.9	−64.0	52.7	53.9	−66.3
C4–C5–C6–O6	−168.2	59.4	−169.7	168.7	58.6	−169.4
O5–C5–C6–O6	69.7	−63.2	69.9	70.2	−63.0	70.6
C5–C6–O6–H	−51.0	49.7	−52.1	−48.7	51.0	−51.1
E	−49.017	−48.686	−40.202	−48.479	−47.427	−41.273
G	438.122	440.069	445.755	436.489	439.038	442.740
ΔE	0.000	0.331	8.815	0.538	1.590	7.744
ΔG	1.633	3.580	9.266	0.000	2.549	6.251
n_i	0.234	0.107	0.011	0.451	0.161	0.035
PEF422						
O5–C1–O1	111.5	111.4	111.5	109.0	108.9	108.8
C5–O5–C1	113.4	113.6	113.5	113.7	113.9	113.9
O5–C1–O1–H	46.6	46.8	45.8	39.2	39.8	−35.9
C1–C2–O2–H	−58.5	−58.7	53.5	53.1	53.5	−179.5
C2–C3–O3–H	−52.4	−51.9	174.9	−54.4	−54.1	171.8
C3–C4–O4–H	52.7	54.4	−61.5	53.1	55.0	−63.7
C4–C5–C6–O6	−166.4	59.3	−167.5	−167.3	58.5	−167.9
O5–C5–C6–O6	71.3	−63.6	71.9	71.5	−63.2	72.1
C5–C6–O6–H	−51.9	51.6	−52.8	−51.4	52.7	−53.4
E	3.891	5.319	14.190	5.945	7.245	10.648
G	490.712	493.669	500.077	490.398	493.281	494.588
ΔE	0.000	1.428	10.299	2.054	3.354	6.757
ΔG	0.314	3.271	9.679	0.000	2.883	4.190
n_i	0.331	0.100	0.008	0.375	0.117	0.069

RESULTS

Table 3 shows conformational and thermodynamic details of the six conformers in all four potential energy functions.

The overall anomer ratios are, for PEF300, PEF301, PEF400 and PEF422: $\alpha:\beta = 0.25:0.75$, 0.32:0.68, 0.35:0.65 and 0.44:0.56. The experimental value, measured by different techniques,[11-15] is 0.36:0.64.

The rotamer ratios for the hydroxymethyl group, ga:g'g, counting both anomers, are for PEF300, PEF301, PEF400 and PEF422: 0.72:0.28, 0.76:0.24, 0.73:0.27 and 0.78:0.22. A compilation[16] for the glucose moiety for about 60 crystal structures gave ga:g'g = 0.40:0.60.

DISCUSSION

Geometric details. Bond lengths, valence angles, endocyclic and hybrid torsional angles show the same deviations from experimental values as in the previous work.[1,2,9]

Two particular angles involving the anomeric carbon atom C1 may be of interest as indicatrices: C5–O5–C1, which is 113.8° in the α[17] and 112.7° in the β[18] anomer, and O5–C1–O1, which is 111.6° in α[17] and 107.0° in β.[18] All four PEF's give a good reproduction of C5–O5–C1 for α, but for β, PEF300 is obviously best, followed by PEF301. For O5–C1–O1, all PEF's give the right trend, but PEF400 and PEF422 the better fit.

As to the exocyclic torsions, at O1, O2, O3 and O4, none changes character (*g*, *g'*, *a*) from one PEF to another. At O6, the simulated hydrogen bond to O5 in PEF400 and PEF422 induces a change from PEF300 and PEF301 in one α and one β conformer.

Thermodynamics. As pointed out before,[3,8,9] it is imperative to sum over internal degrees of freedom when energy differences are as small as here. This point is well illustrated by the ΔE and ΔG data in Table 3.

It may be noted that both α and β are much more homoconformational in the two PEF's with Coulomb terms than in the two without.

The anomeric ratio. The values presented in the previous section were calculated by summation over all six conformers. Therefore they differ, for PEF300 and PEF400, from what was published before,[1-3,9] when only two conformers were considered for PEF300 and four for PEF400. In this respect, now PEF301 gives a significantly better result than PEF300, PEF400 gives still the correct value, and PEF422 overestimates the α anomer to the same extent as PEF300 underestimates it.

Vibrational spectra. Although the results are not shown here, it may be mentioned that the calculated normal modes are very similar in PEF400 and PEF422. The similarity includes even the infrared intensities in the C–H stretching region, in spite of the different charges on C1. This reflects, of course, that no normal coordinate is exclusively localised to any one particular C–H bond.

CONCLUSIONS

The questions asked in the first section can now be answered: (1) The two-parameter Lennard-Jones functions for non-bonded interactions give just as good results as the (theoretically more justified) three-parameter Buckingham exp-6 functions. In the present case, PEF301 with L-J even gives better results in thermodynamic calculations than PEF300 with exp-6.

It is perhaps more surprising that the different charge characteristics of C1 in PEF400 and PEF422 are not reflected in the conformational changes to any significant extent. This result is particularly welcome in the development of PEF's including more types of atoms than those treated here, as one might hope to obtain a reasonably good consistent parameter set with a smaller number of parameters than what would be expected from a theoretical point of view.

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