

CONFORMATIONAL STUDY OF CELLOBIOSE BY QM THEORY

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To gain a better understanding of the effects of intramolecular forces on disaccharide shapes, three regions of the ϕ - ψ space of cellobiose were analyzed with quantum mechanics. A central region, in which most crystal structures are found, was covered by a 9×9 grid of 20° increments of ϕ and ψ . Besides these 81 minimizations that were constrained in ϕ and ψ , we studied two central sub-regions and two regions at the edges of our maps of complete ϕ - ψ space with unconstrained minimization, for a total of 85 target geometries. HF/6-31G* and single-point HF/6-311+G* calculations were used to find the lowest energies for each target. B3LYP/6-31+G* and single point B3LYP/6-311+G* energies for the four regional minima were also computed.

As in the work of Stortz¹, it was important to test many different combinations of exocyclic group orientations (starting geometries). For each of the 85 target geometries, 159 starting geometries were tried that included some redundancy, depending on the criteria for a unique structure. Those starting geometries came from four different methods that were based on molecular mechanics (MM) energies: a conformational search using MacroModel, an erroneous interpretation of the structures reported by Strati et al.², the correct structures from Strati et al. and a facility in Chem-X. (The Strati et al. structures were QM refinements of structures first selected with MM.) Although all four sets contributed to the adiabatic energy map at two or more ϕ - ψ points, use of any single set gave errors of 6 to 10 kcal/mol in this fairly low-energy region of ϕ - ψ space. At the three other levels of theory, other starting geometries gave the lowest energies.

Each of the four levels of theory gave an overall lowest energy structure that is essentially the same as the one found by Strati et al. This structure is in a region that is not well populated by crystal structures, and is more than 3 kcal/mol lower in energy than the populated region. However, it is stabilized by highly cooperative hydrogen bonds. The HF/6-31G* energy contours of the mapped central region were compatible with the observed crystal structures. In particular, two experimental conformations from protein-carbohydrate complexes correspond to lower energies than on empirical energy surfaces. Observed structures that lacked O3 \cdots O5' hydrogen bonds were about 1 kcal/mol above the map's minimum, and relative energies for observed structures that have a pseudo two-fold screw axis were about 0.4 to 1.0 kcal/mol. The HF/6-311+G* map did not accommodate the observed structures as well.

- 1 C.A. Stortz. Disaccharide conformational maps: how adiabatic is an adiabatic map? *Carbohydr. Res.* **322**; 77–86; 1999
- 2 G.L. Strati, J.L. Willett and F.A. Momany. Ab initio computational study of β -cellobiose conformers using B3LYP/6-311++G**. *Carbohydr. Res.* **337**:1833–1849; 2002