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# DFT studies of the disaccharide, α-maltose: relaxed isopotential maps☆

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**Abstract**—The disaccharide, α-maltose, forms the molecular basis for the analysis of the structure of starch, and determining the conformational energy landscape as the molecule oscillates around the glycosidic bonds is of importance. Thus, it is of interest to determine, using density functionals and a medium size basis set, a relaxed isopotential contour map plotted as a function of the $\phi_H$ and $\psi_H$ dihedral angles. The technical aspects include the method of choosing the starting conformations, the choice of scanning step size, the method of constraining the specific dihedral angles, and the fitting of data to obtain well defined contour maps. Maps were calculated at the B3LYP/6-31+G* level of theory in 5° intervals around the $(\phi_H, \psi_H) = (0°, 0°)$ position, out to ~±30° or greater, for *gg–gg′–c*, *gg–gg′–r*, *gt–gt′–c*, *gt–gt′–r*, *tg–tg′–c*, and *tg–tg′–r* conformers, as well as one-split *gg*(*c*)–*gg′*(*r*) conformer. The results show that the preferred conformation of α-maltose in vacuo depends strongly upon the hydroxyl group orientations (‘*c*’/‘*r*’), but the energy landscape moving away from the minimum-energy position is generally shallow and transitions between conformational positions can occur without the addition of significant energy. Mapped deviations of selected parameters such as the dipole moment; the C1–O1–C4′, H1–C1–O1, and H4′–C4′–O1 bond angles; and deviations in hydroxymethyl rotamers, O5–C5–C6–O6, O5′–C5′–C6′–O6′, C5–C6–O6–H, and C5′–C6′–O6′–H′, are presented. These allow visualization of the structural and energetic changes that occur upon rotation about the glycosidic bonds. Interactions across the bridge are visualized by deviations in H(O2)···O3′, H(O3′)···O2, and H1···H4′ distances and the H(O2)–O2–C2–C1 and H′(O3′)–O3′–C3′–C4′ hydroxyl dihedral angles.
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*Keywords:* Disaccharide; Maltose; Density functional; Basis set; Conformation; Isopotential relaxed maps

## 1. Introduction

Conformational analysis of α-(1→4)-linked disaccharides has been a subject of study for many years by a variety of computational methods, with maltose studies recently reviewed.[1] It is not our intention to present another review on the subject, but will refer to several papers closely related to the main subject of this work, that is, mapping the conformational space.[2–10] Most cited papers use classical methods,[2–7] such as molecular mechanics, with empirical force fields. However, ab initio and DFT papers have recently appeared[9–21] examining a variety of carbohydrate structural questions. Our return to mapping the model maltose system is made because of the availability of the rigorous DFT methodology, and because the energy landscape of these important carbohydrates is complicated, and understanding the structural properties of large naturally occurring amylose or starch materials is critical to the development of new materials. Relaxed isopotential maps, often called Ramachandran plots, show where regions of low energy occur in the $\phi_H$ and $\psi_H$ glycosidic bonds torsional space. To be useful, these maps must be predictive and experimental structures should be found in the low-energy regions. In the calculations reported here, the

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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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first B3LYP/6-31+G* density functional isopotential relaxed maps of α-maltose are presented. For the creation of the maps, the glycosidic dihedral angle spacing was chosen with 5° increments, ranging between ~±30° or greater around $(\phi_{\rm H},\psi_{\rm H}) = (0°, 0°)$. The use of a small grid size allows use of continuous segments along an axis without the possibility of large variations in geometry that could occur as the structure is optimized with the $(\phi_{\rm H},\psi_{\rm H})$ dihedral constraints at the desired values. The use of the B3LYP density functional with the 6-31+G* basis set is a compromise between the preferred basis set,[1,11–20] 6-311++G**, and expediency in calculations, a result of the many points on the $\phi_{\rm H}$–$\psi_{\rm H}$ energy surface to be optimized, a decision made to make the connections between points interpolate smoothly. The results of these studies are presented as maps in which the deviations in the energy, and other structure-dependent parameters, are plotted as a function of the $\phi_{\rm H}$ and $\psi_{\rm H}$ dihedral angles.

## 2. Experimental

### 2.1. Computational method

Although the basis set 6-31+G* used here is not as robust as that used 6-311++G** in previous carbohydrate optimization studies,[1,11–20] in combination with the density functional B3LYP,[22] it is fully adequate to prepare high-quality $(\phi_{\rm H},\psi_{\rm H})$ isopotential contour maps where the magnitude of the energy contours falls within a few kcal/mol of the minimum energy, and explicit water molecules are not involved.[19] The basis set relative energy differences were examined previously[19] for the monosaccharide allose and showed only small deviations between the relative energies obtained with the 6-311++G** and 6-31+G* basis sets. Further, energy comparisons taken from the work of Momany et al.[1] are shown here for α-maltose in Figure 1. Figure 1 shows that the deviation in relative energies ($\Delta E$) of the two basis sets are generally within several tenths of a kcal/mol of one another for α-maltose, as indicated by the slope of the fitted line being close to 1.

Parallel Quantum Solutions[23] software and hardware (QS8-2400S, and QS16-2000S) were utilized throughout for $(\phi_{\rm H},\psi_{\rm H})$ constrained energy optimization at each point on the isopotential $\phi_{\rm H}$–$\psi_{\rm H}$ map. Convergence criteria were similar to those used for previously published saccharides[1,11–21] with an energy change of less than $1 \times 10^{-6}$ Hartree and a gradient of less than $3 \times 10^{-4}$ a.u. The computed Hessians during optimization did not show negative eigenvalues, indicating that the optimized structure is at a local minimum under the given $(\phi_{\rm H},\psi_{\rm H})$ dihedral constraint. Results have been displayed using HYPERCHEM[24] v7.5 and ORIGIN[25] v7.5, with the contour maps created by interpolative methods between grid points. The standard numbering scheme for sugars was used and is displayed for clarification in Figure 2.

### 2.2. Isopotential and isogeometric contour maps

From previous[1] DFT optimization studies of α-maltose conformations, it is clear that several different exocyclic

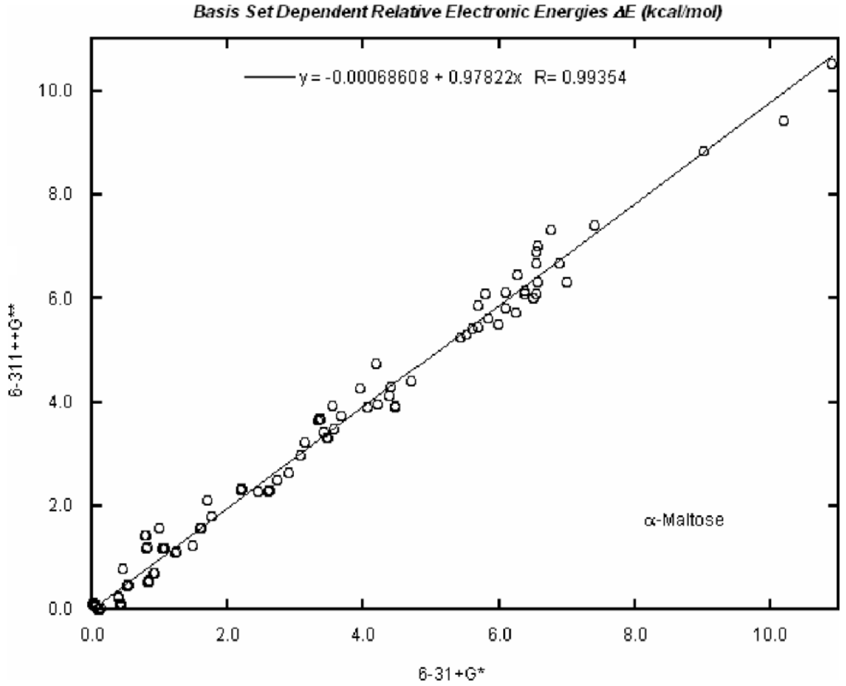

**Figure 1.** Plot of optimized relative electronic energies ΔE (kcal/mol) of α-maltose conformations for B3LYP/6-311++G** versus B3LYP/6- 31+G*.