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A theoretical study of structures of hexopyranose anomers using QM/MM method

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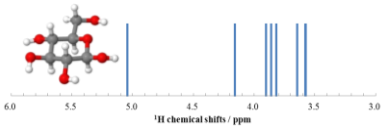
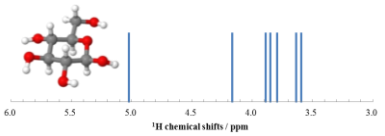
Hexose such as glucose generally exists as a pyranose form. Hexopyranose has 5 asymmetric carbon atoms and has many stereoisomers. Especially, anomer (α or β) is stereoisomer on C1 atom of hexopyranose. In aqueous solution at room temperature, it was experimentally observed [1] that glucopyranose (Glc) exists as a mixture of α : β = 36 : 64, while mannopyranose (Man) exists as a mixture of α : β = 68 : 32. The existence ratio between the α- and β-anomers of a hexoppyranose is very sensitive to solvent and the origin of the difference between hexopyranoses has not been clarified yet. In this study, we reveal structures and stabilities of Glc and Man in aqueous solution.

QM/MM–MD method was performed for the systems of hexopyranose (treated as QM) in aqueous solution with the following conditions: the number of MM water molecules was 148, a time step of MD was 0.2 fs and the total number of steps was 10000 at 300 K (NVT ensemble). XYZ coordinates of the system at some steps were extracted and were optimized. The geometries of hexopyranose optimized in the gas phase (geom-g) and using QM/MM method (geom-w) were optimized using PCM method (geom-g-p and geom-w-p, respectively). For these 4 types of geometries, ^{1}H NMR chemical shifts and IR frequencies were calculated (in the gas phase and with PCM).

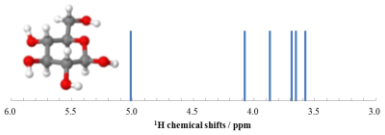
By QM/MM–MD followed by QM/MM optimization procedure, we found that β-anomer is more stable than α-anomer for Glc, and that α-anomer is more stable than β-anomer for Man. These results are consistent with experimental observations. The geometries optimized using QM/MM method have different directions of OH groups from those optimized in the gas phase. As shown in the Figure, ^{1}H chemical shifts based on geom-w are consistent with experimentally observed ^{1}H chemical shifts [2]. ^{1}H chemical shifts of geom-g, geom-g-p and geom-w-p are different from the experimental observation. These results indicate that it is needed to consider solvent molecules explicitly for calculations of hexopyranose in aqueous solution.



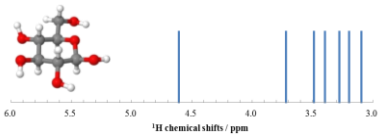
(a) geom-g



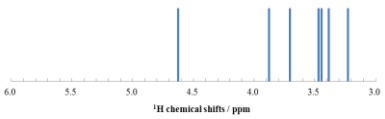
(b) geom-g-p



(c) geom-w-p



(d) geom-w



(e) experiment [2]

Figure. Computational ((a) – (d)) with PCM and experimental (e) ^{1}H NMR spectra (schematically drawn) of β-Glc.

[1] Angyal, S. J. *Angew. Chem. In. Ed. Engl.* **8**, 157-166 (1969).

[2] Roshind, M. U., Tahtinen, P., Niemitz, M. & Sjhohn, R. *Carbohyd. Res.* **343**, 101-112 (2008).