A DFT study of the influence of nature and position of substituents on monosaccharide conformations – $^4C_1$ – $^1C_4$ chair equilibria in acylated xylose

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The influence of both nature (acetyl *vs.* benzoyl) and position (2,4-diacyl *vs.* 3,4-diacyl) of acyl-substituents on the ring conformation ($^4C_1$, $^1C_4$ chairs, ^2S_O skew boat) of methyl ß-D-xylopyranoside derivatives is investigated by computational procedures (DFT using various functionals (B3LYP, MPWB1K, M05-2X) and ab initio (MP2)). In the 2,4-diacyl derivatives, especially for methyl ß-D-2,4-dibenzoylxylopyranoside, the stability of the $^1C_4$ compared with the usually found $^4C_1$ chair increases with decreasing solvent polarity (H_2O < DMSO < $CHCl_3$ < CCl_4). This increased stability of the $^1C_4$ can mainly be attributed to the presence of an intramolecular hydrogen bond O3–H3 ··· O1. In 3,4-diacyl derivatives no such intramolecular hydrogen is possible, hence, the $^4C_1$ ring conformation is prevalent even in CCl_4. Comparing acetyl *vs.* benzoyl groups, the latter one is calculated to induce a shift towards the $^1C_4$ chair in agreement with experimental results (although experiments concerning the effect of substituents on xylose conformations yield conflicting results!). Most probably, this effect of the benzoyl groups can be attributed to sorts of stacking interactions between the two aromatic rings, actually with a T-shaped arrangement. Not surprisingly, then, B3LYP results are not very reliable for these derivatives in contrast to the diacetyl methyl ß-D-xylopyranoside isomers. Spin component scaled MP2 results are in better agreement with experimentally determined conformer populations than those derived from MP2 calculations.