The complete description of the conformational behaviour of sugars involves assessing
exocyclic dihedral angles and ring conformations, both in terms of static conformations
and dynamic behaviour within these limiting conformers. We have focused here on the
conformation of the tetrahydrofuran ring and its deviation from planarity. Beyond the
well-known pseudo-rotational analysis based on two parameters, puckering angle and
amplitude, we present a complementary and new approach to describe ring conforma-
tional dynamics which is better able to describe unsymmetrical conformations that are
lost by pseudo-rotational analysis. Principal Component Analysis (PCA) of the endocyclic
dihedral angles proved to be an efficient method to describe collective, global motions of
the carbohydrate ring, with two or three principal components containing the largest
mean-square fluctuation. Our ring dihedral principal component analysis model (RdPCA)
describes ring conformational dynamics based on inherent ring motions rather than
arbitrarily restrictive descriptors. RdPCA analysis of both classical and full quantum
mechanical molecular dynamics indicates that furanosides have dominant minimum
energy conformations but are rather flexible within these conformers, showing broad
wells from a thermodynamic point of view. This RdPCA model also gave indications on the
kinetic behaviour of such systems suggesting possible energy pathways for ring motions
on the energy landscape. We believe that this useful tool can give a better understanding
of the behaviour of the tetrahydrofuran ring, and hence of carbohydrate conformation.

1 Introduction

The understanding of carbohydrate conformation and dynamics is a
central issue in carbohydrate recognition, pharmacology, and stereo-
selective synthesis. The importance of conformation in carbohydrate
recognition has been widely recognized since the 1970’s, with the pion-
eering work of Lemieux and others. More recently, the rapidly growing
implication of carbohydrates in the pharmaceutical industry, from
traditional aminoglycoside antibiotics and nucleoside analog antiviral
and antitumor agents, to heparin-based pentasaccharides (Fondiparinux
and Idraparinux), synthetic vaccines, lipid A analogs (eritoran tetra-
sodium), KRN 7000 analogs, glycosidase inhibitors (Glucobay, Glyset,
Miglustat, Oseltamivir), and glycoside alkaloids have brought the
conformational analysis of carbohydrates to the forefront of drug
design. Finally, from the chemical point of view, an understanding of