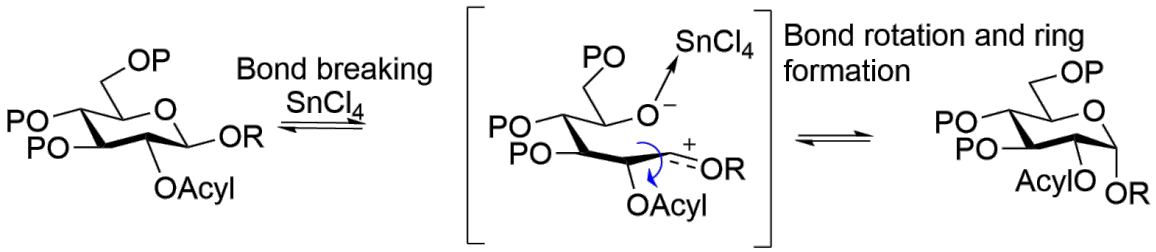
Study of $SnCl_4$ promoted anomerisation via endocyclic cleavage using LFERs and DFT calculations

Paul MURPHY [1], Fiach MEANY [1], Louise KERINS [1]

[1] School of Biological and Chemical Sciences, University of Galway, University Road, Galway, Ireland

paul.v.murphy@universityofgalway.ie

Anomerisation is used to convert equatorial glycosides to axial glycosides and the mechanism is proposed to involve endocyclic cleavage, followed by a bond rotation and ring reformation step. Rates of $SnCl_4$ promoted anomerisation were determined for 14 glucopyranosides, 12 glucuronic acid and 16 galacturonic acid derivatives to deduce the influence of 2-O-acyl groups on reactivity. Linear correlations for 2-O-benzoyl derivatives in plots of log k_f+k_r vs Hammett sigma$^+$ parameters were observed. Increasing the size of aliphatic 2-O-acyl groups led to an increase in rate for galactopyranosiduronic acid and glucopyranose, but not for glucopyranosiduronic acid. Plots of steric parameters such as Pavelich-Taft E_S or Verloop's Sterimol B1 vs log k_f+k_r indicate a correlation between size and rate. Taft's polarizability parameter sigma$_a$ was correlated with log k_f+k_r, for aliphatic substituents and may indicate that increased polarizability, which is related to the size of the aliphatic substituent is consistent with an increase in reactivity and could contribute. DFT study has been used to establish mechanistic pathways for the glucopyranosides and glucuronic acid. The pathways first involve carbocation intermediate formation followed by a high energy bond rotation step, likely to be rate determining. Contributions from 2-acyl group participation are evident but the protecting group role differs depending on the reacting glycoside. These data and mechanistic pathway will be discussed along with relative energies of intermediates and transition states.



Anomerisation of glucopyranoside

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Bibliographic references:

1. For a review see P. V. Murphy, (2016) Carbohydr. Chem. 41, 90.