

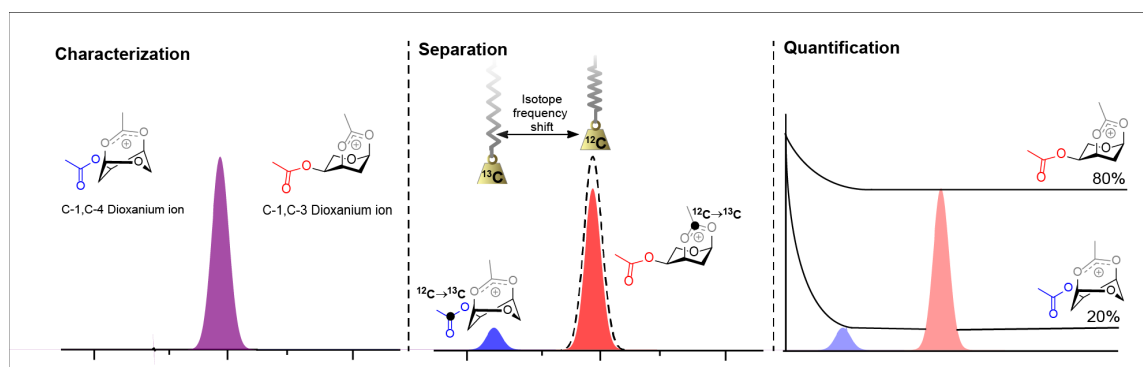
## Exploration of long range participation in 3,4-diacetylated glycosyl donors

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The key challenge in chemical oligosaccharide synthesis is the stereoselective installation of glycosidic bonds. Each glycosidic linkage has two stereo-outcomes,  $\alpha/\beta$  or *cis/trans* and is affected by the reaction mechanism operating on a SN1-SN2 continuum. One of the most established approaches to reliably install 1,2-*trans* glycosidic bonds is neighboring group participation (NGP) mediated by a 2-O-acyl group. Through formation of a transient bicyclic intermediate, the C-1,C-2 dioxolenium ion, effectively one face of attack is shielded which enhances reaction stereoselectivity. The extension of this intramolecular stabilization to nucleophilic groups located at more remote positions has also been suggested but remains a controversial topic and is poorly understood. However, to improve the stereoselective synthesis of glycans, characterizing these highly-reactive intermediates and understanding their role in glycosylation mechanisms is crucial. Previously, we employed infrared ion spectroscopy to characterize the molecular ions of monoacetylated sugar donors and showed how the strength of the stabilizing effect depends on the position of the participating ester group on the glycosyl donor ring as well as its relative stereochemistry. In this work, we extended this workflow towards diacetylated glycosyl donors. This study highlights the potential of isotope labelling in resolving spectra of compounds bearing multiple structurally similar functional groups. In combination with population analysis a powerful combination is created that allows one to disentangle isomeric mixtures and establish the relative contribution of individual isomers.



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### Bibliographic references:

- Braak, Floor ter, et al. (2022), *Accounts of Chemical Research* 55.12 1669-1679.  
 Hansen, Thomas, et al. (2020), *Nature Communications* 11.1: 2664.  
 Elferink, Hidde, et al. (2022), *Chemistry—A European Journal* 28.63: e202201724.  
 Remmerswaal, Wouter A., et al. (2022), *The Journal of Organic Chemistry* 87.14: 9139-9147