Synthesis and Computational Modeling of Sucrose-based Phytochemicals as Lead Pharmaceutics

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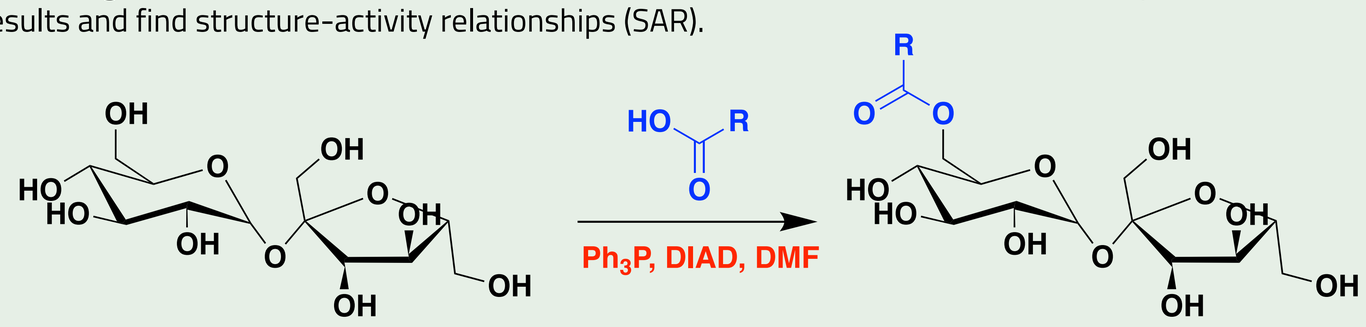
What we know so far

Carbohydrates are indispensable components for living systems, providing nourishment, energy, and even contributing to the treatment of various diseases. However, there are still few drugs containing carbohydrates on the market and more research efforts need to be done, particularly on those derived from sucrose. [1,2] Phenolic Sucrose Esters (PSEs) are a class of bioactive compounds, traditionally employed in folk medicine and sourced from various plants, known for their anti-proliferative, antioxidant, anti-inflammatory, and α-glucosidase inhibitory properties. Very few of these have been obtained synthetically, which, combined with the milligram quantities isolated from plants in pure form, has prevented their use in pharmacology. [3,4] Initially identified in *Raphanus sativus* (Figure 1), PSEs have since been discovered in various plant species frequently used in alternative medicine, such as *Veronicastrum sibiricum* (Figure 2), *Musa acuminata*, *Polygala sibirica*, among others. [5] With this project, we explored one-step selective chemical methodologies (Mitsunobu conditions) to synthesize **24 biologically active sucrose esters** (6 monoesters, 6 per-acetylated monoesters, 6 diesters and 6 per-acetylated diesters) with very promising applications (Scheme 1). A part of the project includes a computational estimation of the radical scavenging effects of these compounds through different reaction pathways - hydrogen atom transfer (HAT), single electron transfer (SET) and radical adduct formation (RAF). Then, we will perform *in-vitro* studies to determine experimentally the antioxidant activities to compare the results and find structure-activity relationships (SAR).

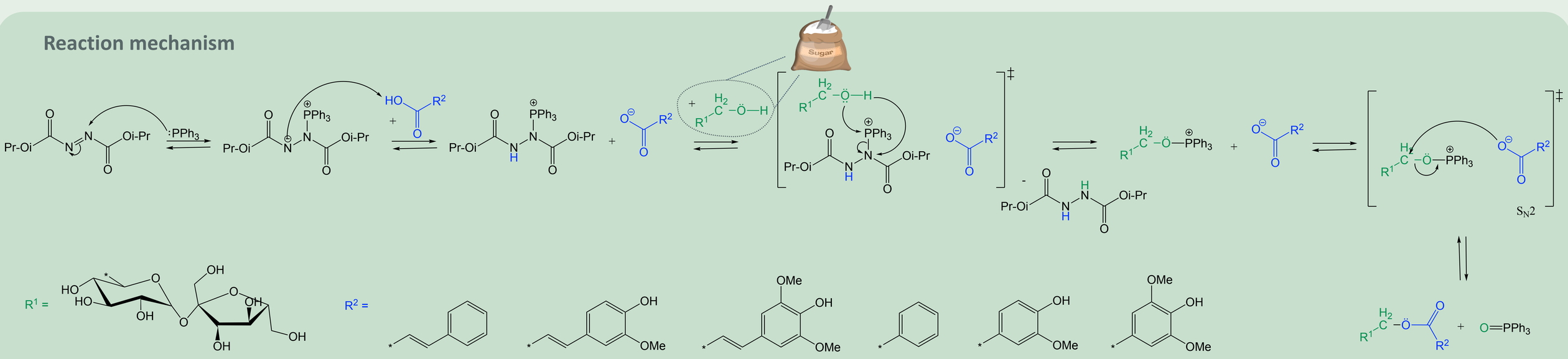
Figure 1: *Raphanus sativus*



Scheme 1: Acylation of sucrose under Mitsunobu conditions.

Figure 2: *Veronicastrum sibiricum*

Reaction mechanism



Scheme 2: Complete mechanism, proposed by us, of acylation of sucrose under Mitsunobu conditions.

Results

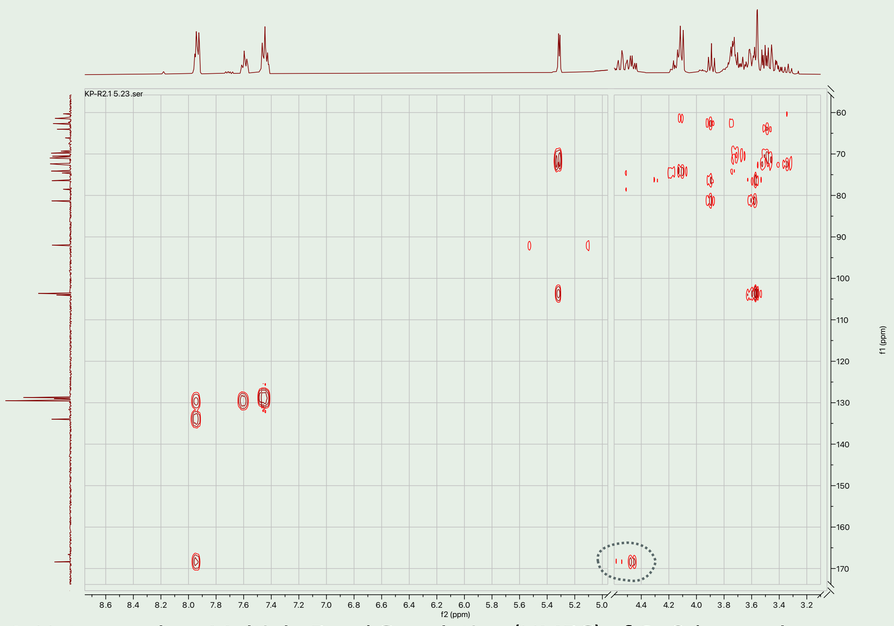


Figure 1: Heteronuclear Multiple Bond Correlation (HMBC) of 6-*O*-benzoyl sucrose ester.

The HMBC can identify a correlation between the C in the ester bond and the C6-H proton, confirming a regiospecific 6-OH acylation of sucrose.

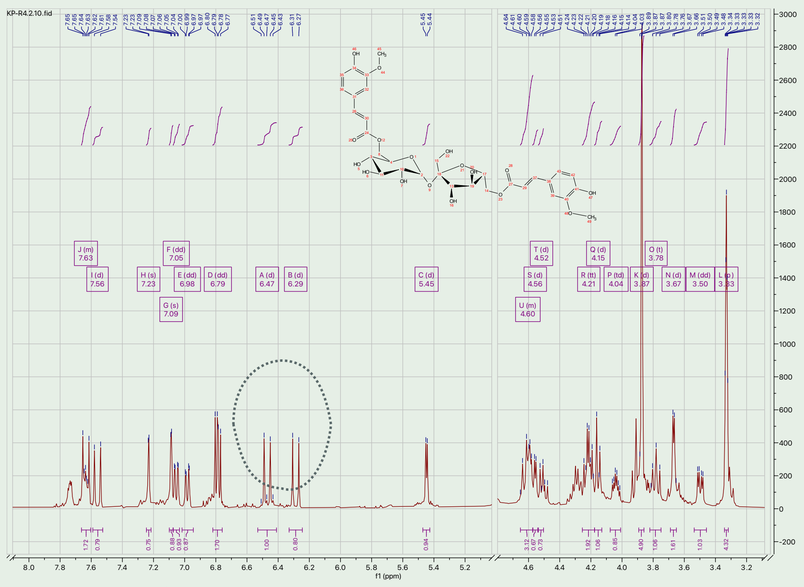
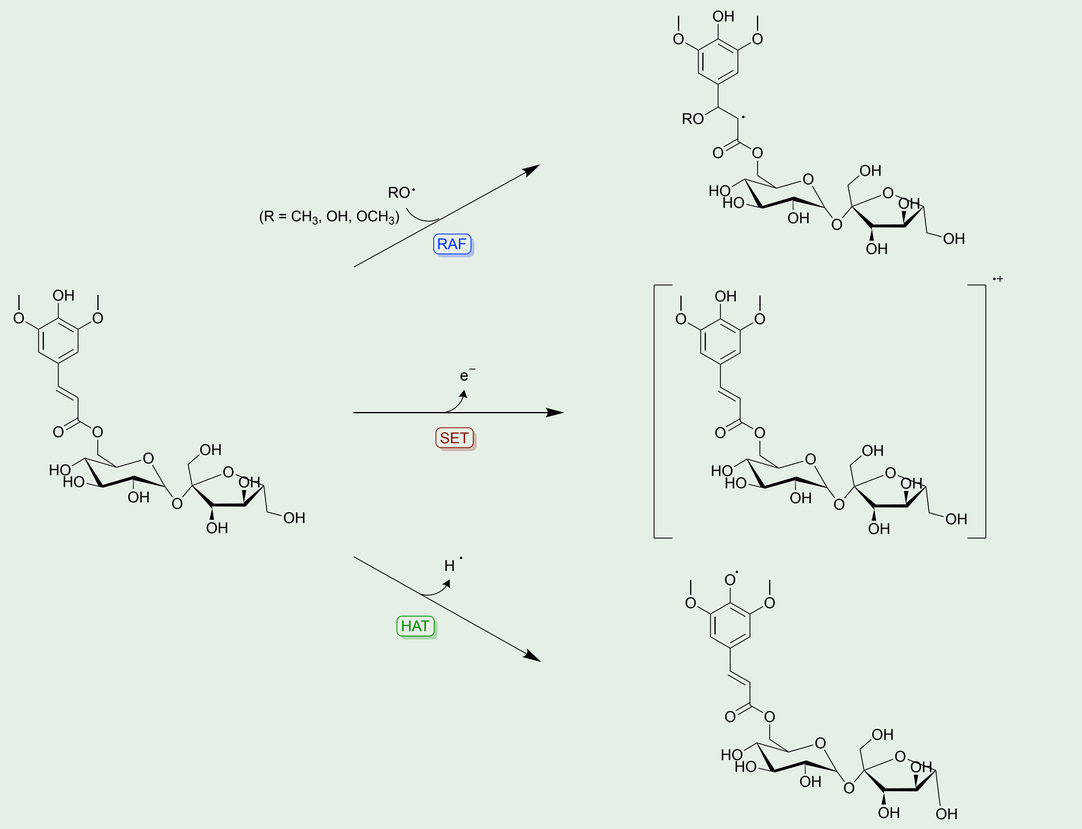


Figure 1: ^{1}H NMR spectrum of 6,6'-di-*O*-feruloyl sucrose ester.

The duplets at 6.29 ppm and 6.47 ppm correspond to the double bonds of ferulic acid close to the ester groups.

Next tasks



Scheme 3: Possible mechanisms of radical-scavenging activity of 6-*O*-sinapoyl sucrose ester.

Conclusions

So far, we have successfully synthesised half of the target compounds with yields up to 33%. The regioselective 6-OH acylation can be confirmed by the HMBC. It is important to note that we succeeded the first synthesis of 6-*O*-benzoyl sucrose ester and of 6,6'-di-*O*-feruloyl sucrose ester.

Acknowledgements

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References

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