# Leveraging Non-classical σ-hole based Noncovalent Interactions and Asymmetric Catalysis: Emerging Frontiers in Stereoselective Carbohydrate Synthesis

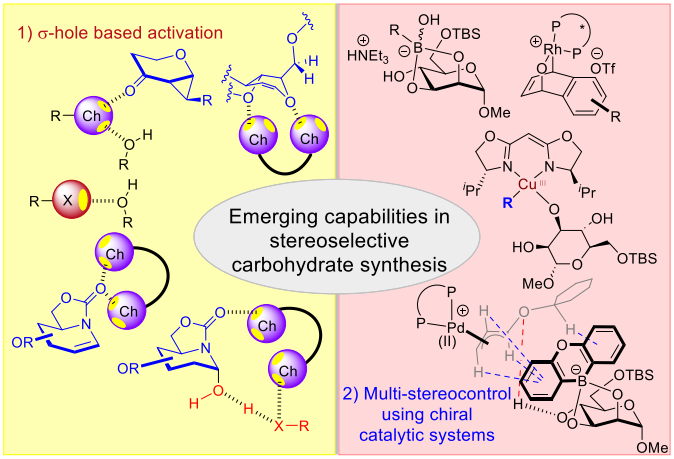
Charles C. J. Loh
UCD School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland.
charles.loh@ucd.ie

There is a recent renaissance amongst organic chemists in appreciating the value of stereoselective carbohydrate synthesis as an excellent platform for discovery of chemical phenomena.[1] In my talk, I will describe two emerging directions pursued by my research group.

In the first direction, I will narrate our seminal efforts in developing mild and robust *σ*-hole based noncovalent catalyzed methods for selective carbohydrate synthesis – an approach we now define as the "*σ-hole based catalytic glycosylation strategy*".[2-3]

I will offer an overview of our early efforts in the development of exclusively halogen bonding (XB) catalyzed strain-release glycosylation[4] and 2-deoxyglycosylation.[5] These strategies contain unique advantages, such as the elevation of anomeric selectivity. Next, I will introduce our pioneering approach in chalcogen bonding (ChB) catalyzed glycosylations and glycomimetic synthesis. We recently demonstrated that the ChB catalysis performed exceptionally well on glycosyl substrates. We further developed versatile strategies that enabled access into biologically relevant 7-membered ring sugars known as septanosides,[6-7] β-indolyl glycosides[8] as well as in underexplored iminoglycosides.[9]

A second research axis is the harnessing of metal catalyzed asymmetric catalysis to surmount multiple enantio-, diastereo- and site-selectivity challenges within a single bond forming step.[2] Besides sharing novel asymmetric rhodium[10] and radical copper catalyzed[11] platforms we developed, I will touch on recent efforts to exploit NCIs for carbohydrate stereocontrol in the context of asymmetric palladium catalyzed site-selective functionalizations.[12] By bridging supramolecular chemistry, physical organic chemistry, catalytic method development and carbohydrate chemistry, we believe that innovative solutions to tackle long-standing stereoselectivity problems can be discovered at the interface of these fields.




**References:**
1. C. C. J. Loh, *Angew. Chem. Int. Ed.* **2025**, DOI: 10.1002/anie.202514167
2. A. T. Sebastian, C. C. J. Loh, *Acc. Chem. Res.* **2025**, 58, 2124-2144.
3. C. C. J. Loh, *Nat. Rev. Chem.* **2021**, *5*, 792-815.
4. C. Xu, C. C. J. Loh, *J. Am. Chem. Soc.* **2019**, *141*, 5381-5391.
5. C. Xu, V. U. Bhaskara Rao, J. Weigen, C. C. J. Loh, *Nat. Commun.* **2020**, *11*, 4911.
6. W. Ma, J-L. Kirchhoff, C. Strohmann, B. Grabe, C. C. J. Loh, *J. Am. Chem. Soc.* **2023**, *145*, 26611-26622.
7. W. Ma, A. Schmidt, C. Strohmann, C. C. J. Loh, *Angew. Chem. Int. Ed.* **2024**, *63*, e202405706.
8. H. Guo, J-L. Kirchhoff, C. Strohmann, B. Grabe, C. C. J. Loh, *Angew. Chem. Int. Ed.* **2024**, *63*, e202316667.
9. C. Wang, A. Krupp, C. Strohmann, B. Grabe, C. C. J. Loh, *J. Am. Chem. Soc.* **2024**, *146*, 10608-10620.
10. V. U. Bhaskara Rao, C. Wang, D. P. Demarque, C. Grassin, F. Otte, C. Merten, C. Strohmann, C. C. J. Loh, *Nat. Chem.* **2023**, *15*, 424-435.
11. H. Guo, D. Tan, C. Merten, C. C. J. Loh, *Angew. Chem. Int. Ed.* **2024**, *63*, e202409530.
12. H. Guo, J-L. Kirchhoff, C. Strohmann, B. Grabe, C. C. J. Loh, *Angew. Chem. Int. Ed.* **2024**, *63*, e202400912.