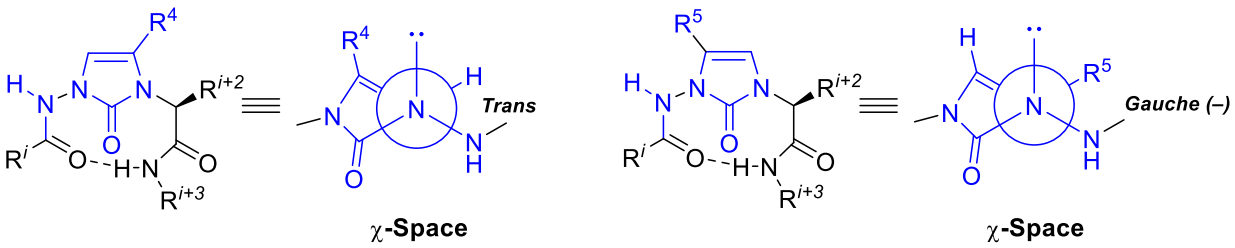
N-Aminoimidazole-2-ones peptide mimics

Y. Hamdane[a], P. S. Chauhan[a], S. Vutla[a], D. Truong[a], D. Mulumba[b], H. Ong[a], W.D. Lubell[a]

[a]Department of Chemistry, and [b]Faculty of Pharmacy, Université de Montréal, Montréal, QC, Canada

α-Amino lactam (Agl) units have served as conformational constraints in peptide-based drug discovery since the pioneering studies of Freidinger and Veber [1]. In peptides, Agl residues have been shown to adopt the *i* + 1 position of β-turn secondary structure which play privileged roles in molecular recognition. *N*-Aminoimidazolone (Nai) residues offer similar means for constraining peptide backbone geometry in β- and γ-turn conformers and are apt for functionalization with substituents to study side chain orientation [2].



Our presentation discusses a general organocatalytic method for the synthesis of 4-, 5- and 4,5-substituted Nai dipeptides [3,4]. The synthesis and application of substituted Nai dipeptides will be showcased in structure-activity relationship studies of cluster of differentiation-36 receptor ligands that act as modulator of inflammation [3,4].

1. Freidinger, R. M. Design and Synthesis of Novel Bioactive Peptides and Peptidomimetics *J. Med. Chem.* **2003**, *46*, 5553- 5566.
2. St-Cyr D.J., García-Ramos Y., Doan N.D., Lubell W.D. *Peptidomimetics I.* Springer; Cham, Switzerland: 2017. Aminolactam, *N*-Aminoimidazolone, and *N*-Aminoimdazolidinone Peptide Mimics; pp. 125–175.
3. Hamdane, Y.; Poupart, J.; Lubell, W. D. *Synthesis*, **2022**, *54* (6), 1518–1526.
4. Hamdane, Y.; Chauhan, S. P.; Vutla, S.; Mulumba, D.; Ong, H.; Lubell, W. D. *Org. Lett.* **2021**, *23* (9), 3491–3495.