



Defining peptide structure and enzyme function: A metathesis approach

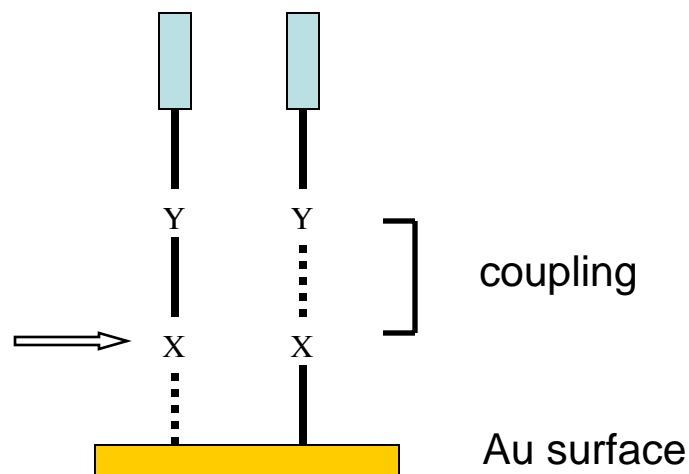
Invited talk Abstract

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The structure and function of a protein is defined by the combination of its secondary, tertiary, and in some cases quaternary structure. These higher and functional levels of structure are themselves defined by the nature of the proteins constituent amino acids. Here we describe our work on using metathesis to define and mimic natural and non-natural amino acid and peptide structure in solution and on surfaces, with a view to understanding and exploiting protein structure and function. These ideas have been extended to develop a potential pharmaceutical treatment for cataract based on the inhibition of a cysteine protease found in the lens of an eye. Aspects of this study, from inception through to the commercial interface, are discussed.

Metathesis surface attachment



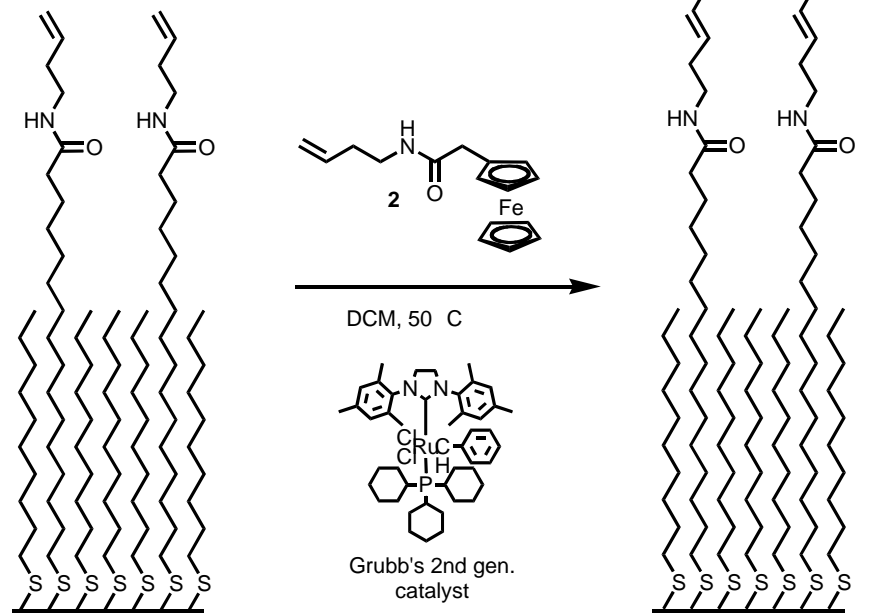
Cross metathesis

Click chemistry

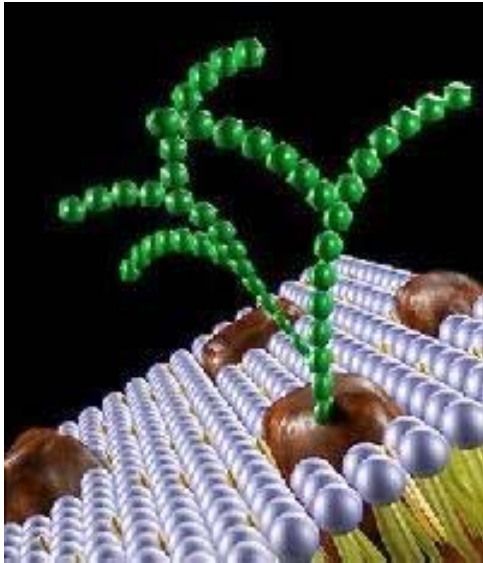
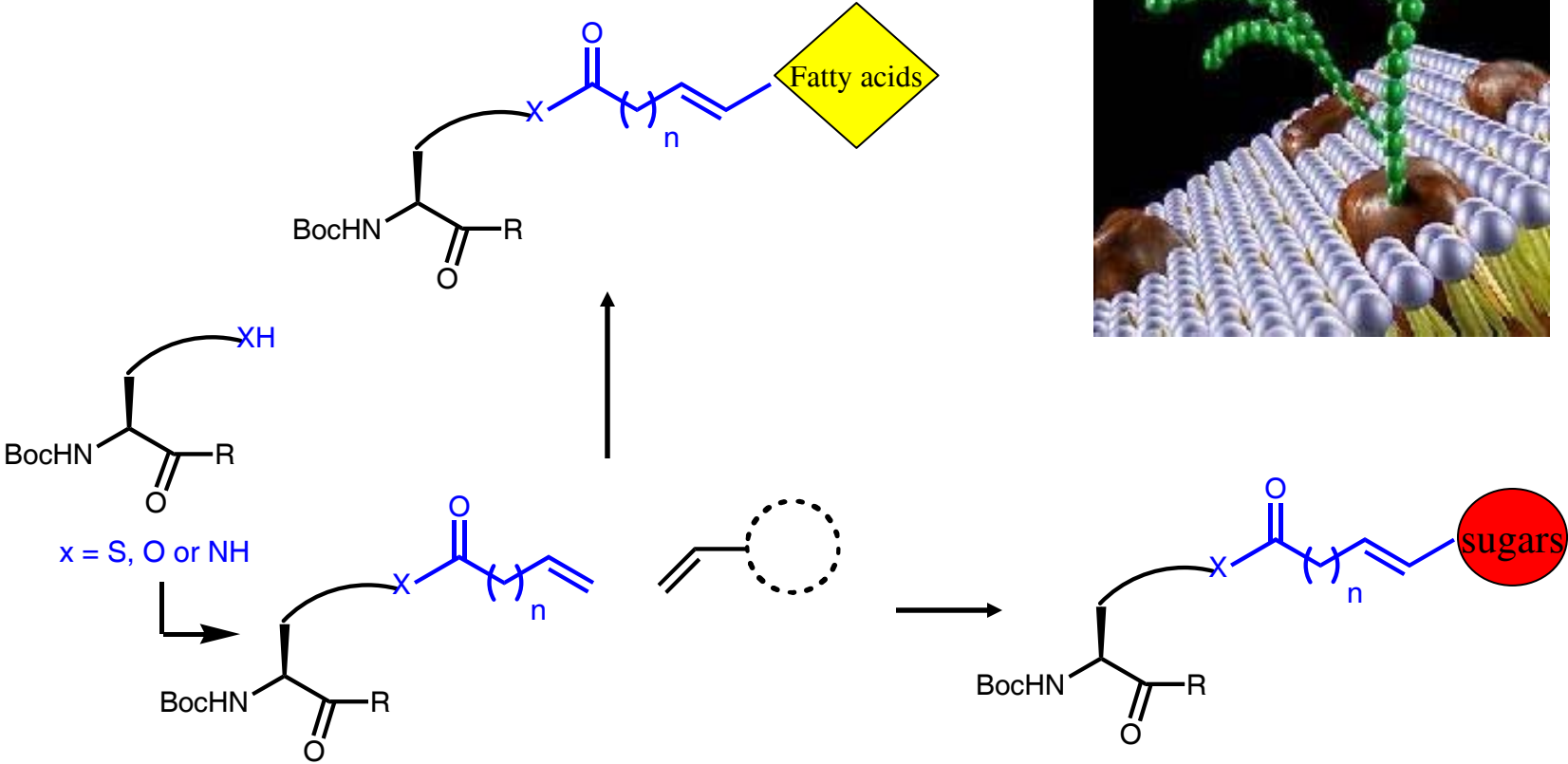
Cross metathesis

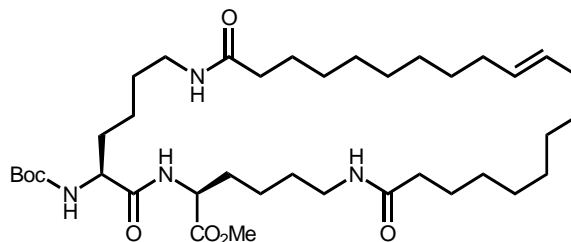
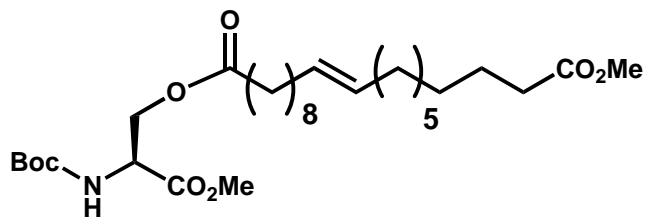
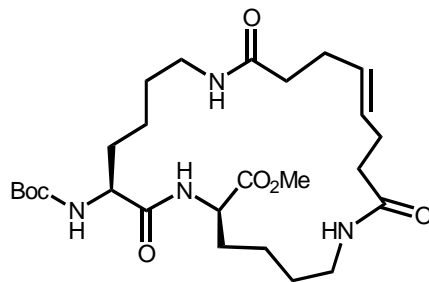
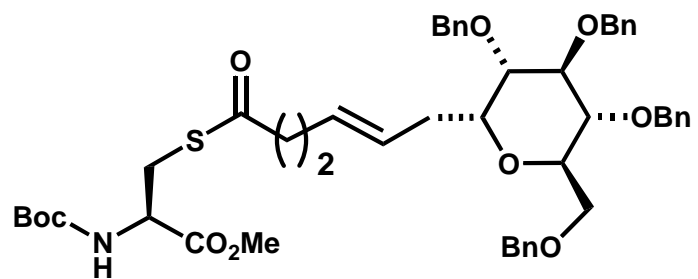
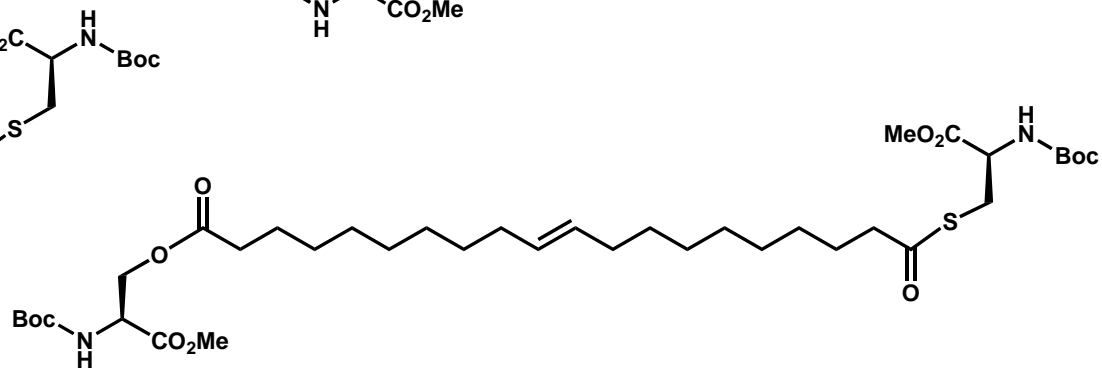
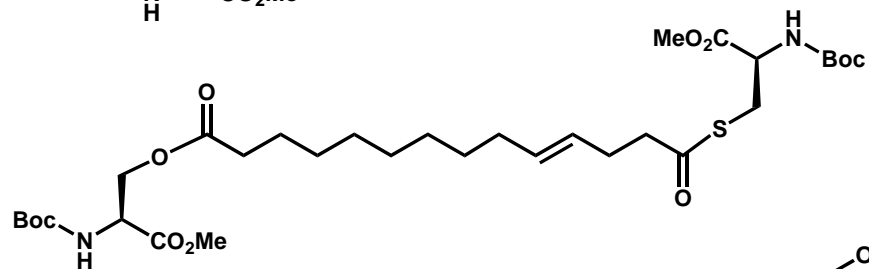
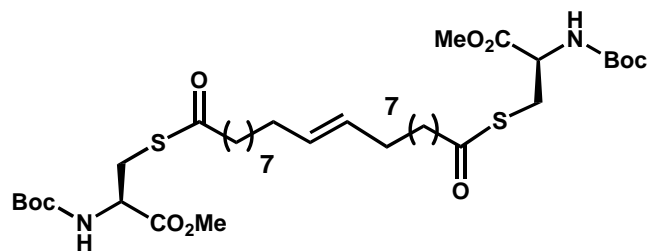
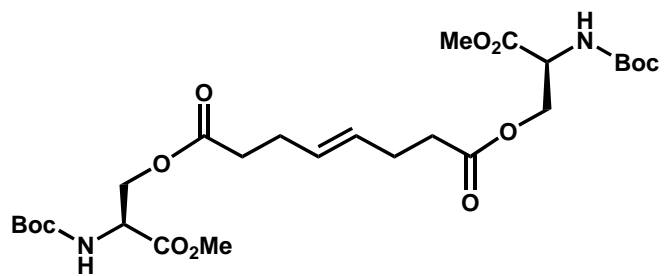
$n = 4, 9, 15$ diluents

Gold electrode



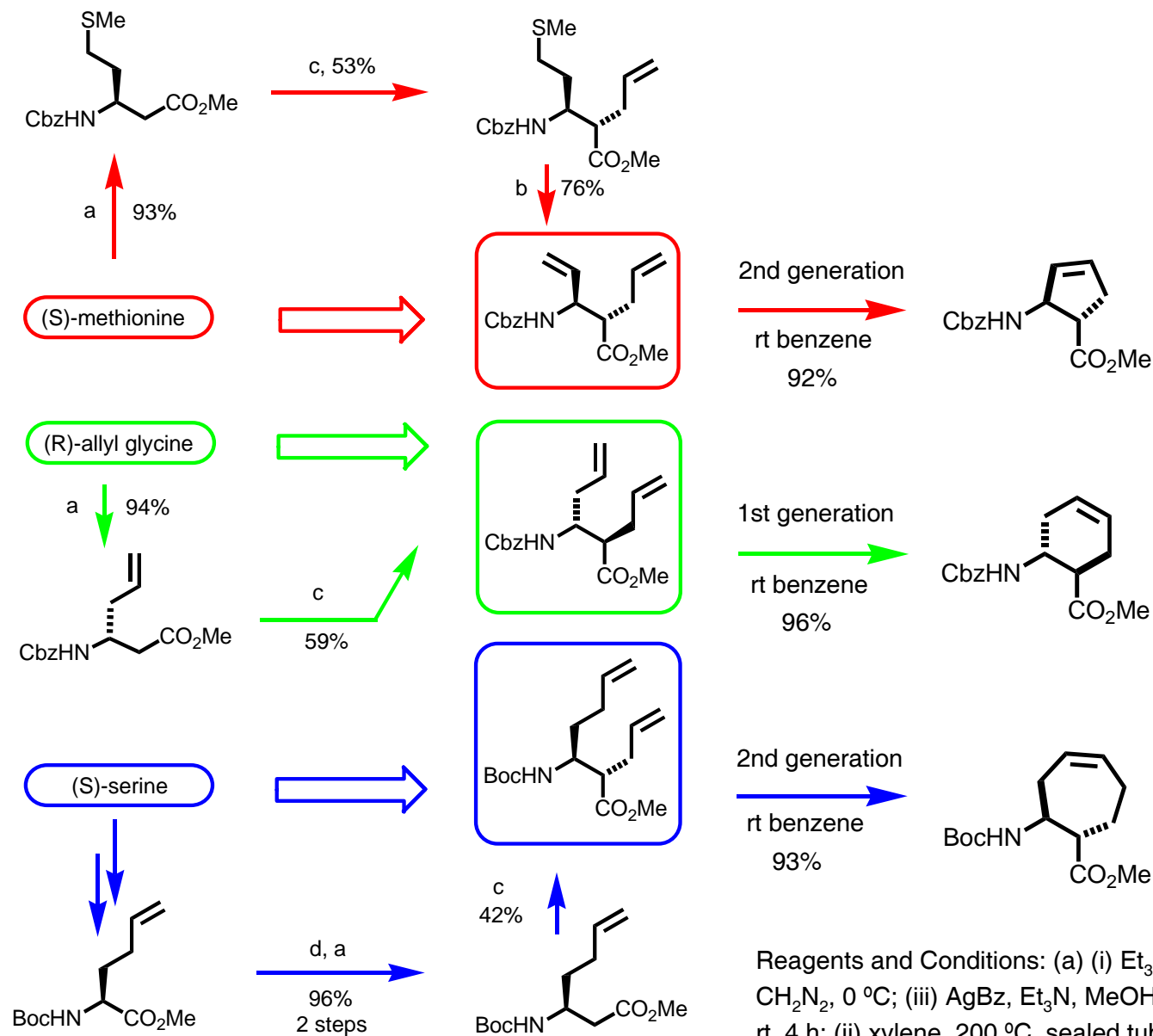
Glycoproteins and glycolipids





Andrea Vernall

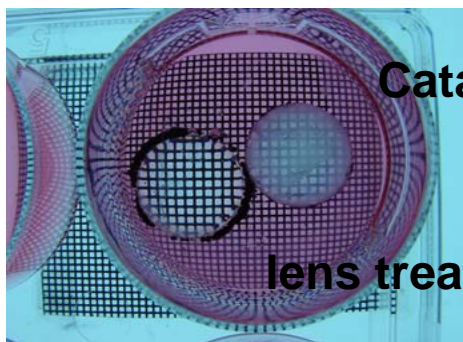
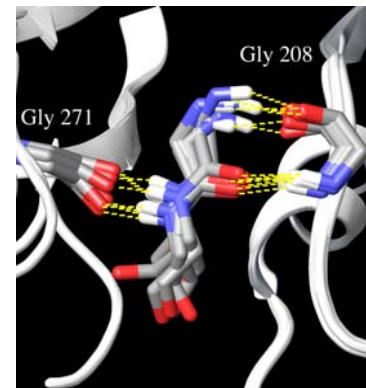
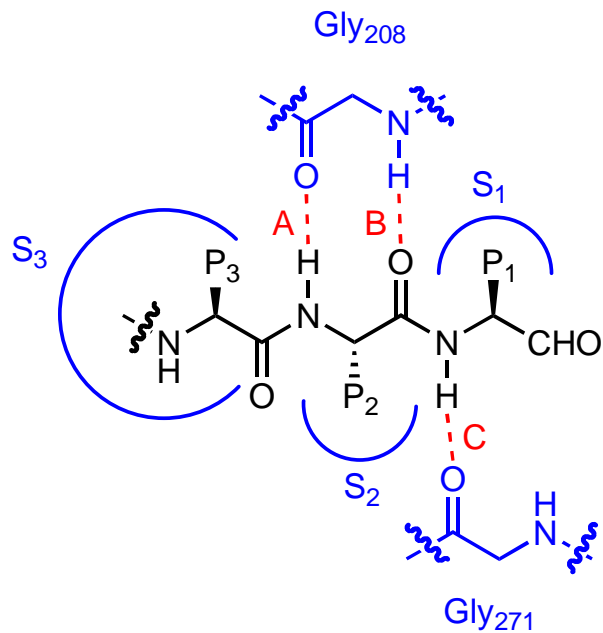
Cyclic β -amino acids derived from α -amino acids



Reagents and Conditions: (a) (i) Et_3N , ClCO_2Et , THF, -15°C ; (ii) CH_2N_2 , 0°C ; (iii) AgBz , Et_3N , MeOH, -25°C ; (b) (i) H_2O_2 , AcOH, rt, 4 h; (ii) xylene, 200°C , sealed tube; (c) LiCl, 2 equiv of LDA, allyl bromide, THF, -78°C ; (d) NaOH, MeOH, reflux.

β -Strand mimetics: protease inhibitors to treat cataract

Protease inhibitors bind to S1, S2 and S3 subsites in an anti-parallel β -strand conformation.



Cataract lens

lens treated with cataract inhibitor prepared by RCM