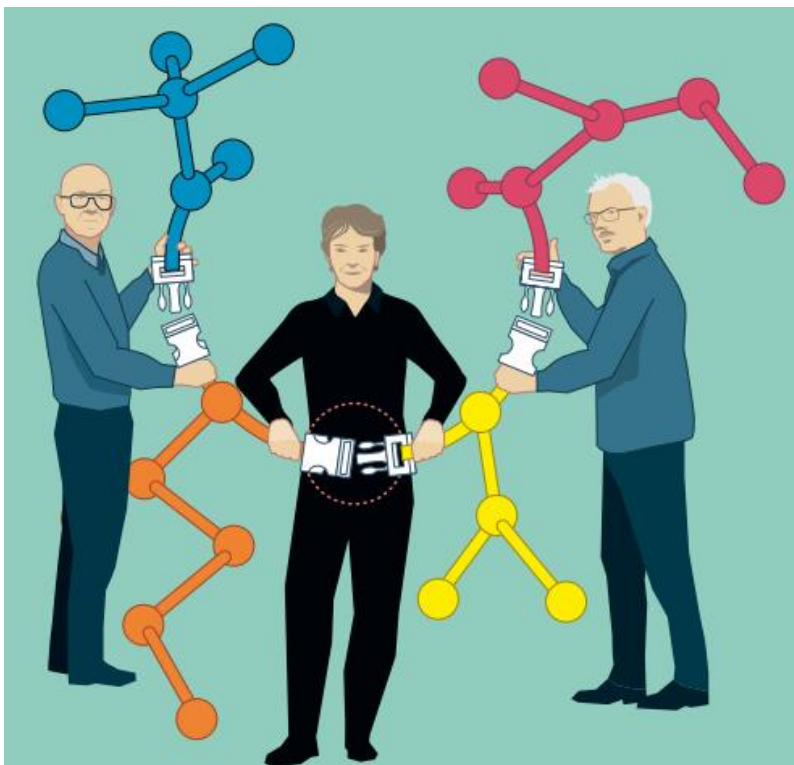
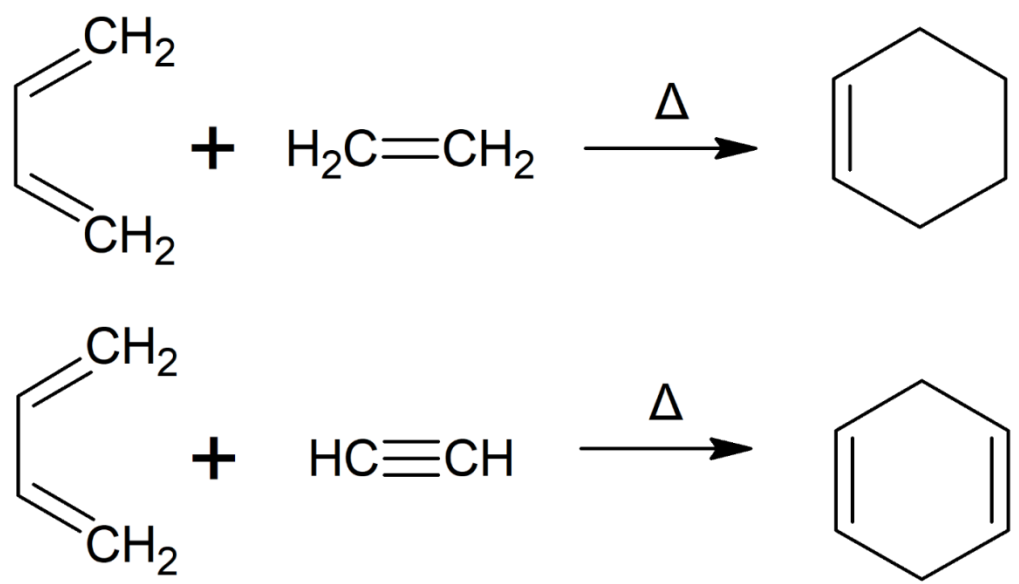


The Nobel Prize in Chemistry 2022

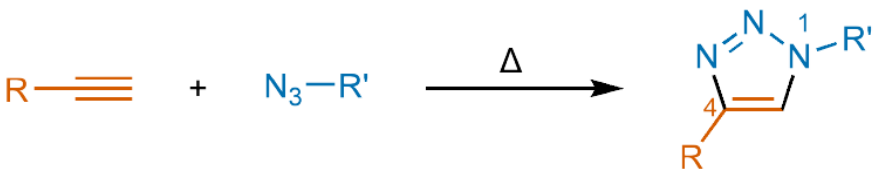


The Nobel Prize in Chemistry 2022 The Nobel Prize in Chemistry 2022 was awarded jointly to Carolyn R. Bertozzi, Morten Meldal and K. Barry Sharpless "for the development of **click chemistry** and **bioorthogonal chemistry**"

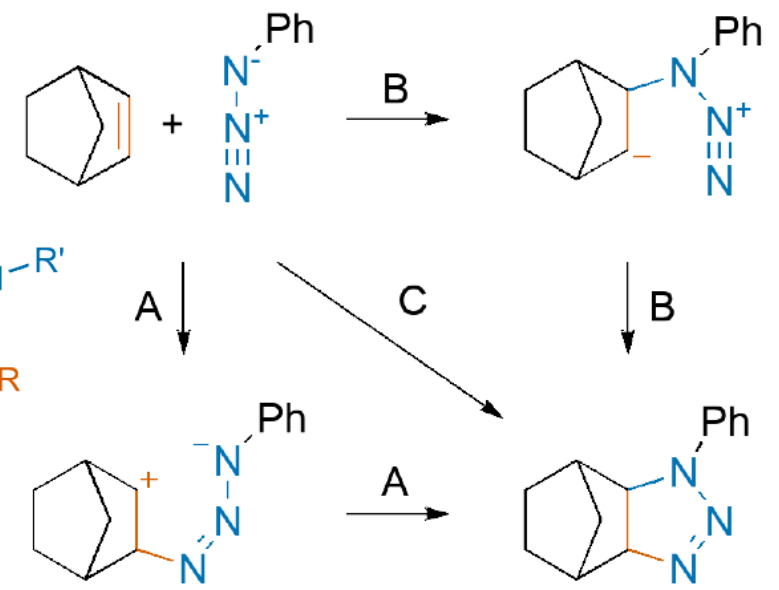
[4+2] Diel-Alder Cycloaddition: Nobel Prize in Chemistry 1950



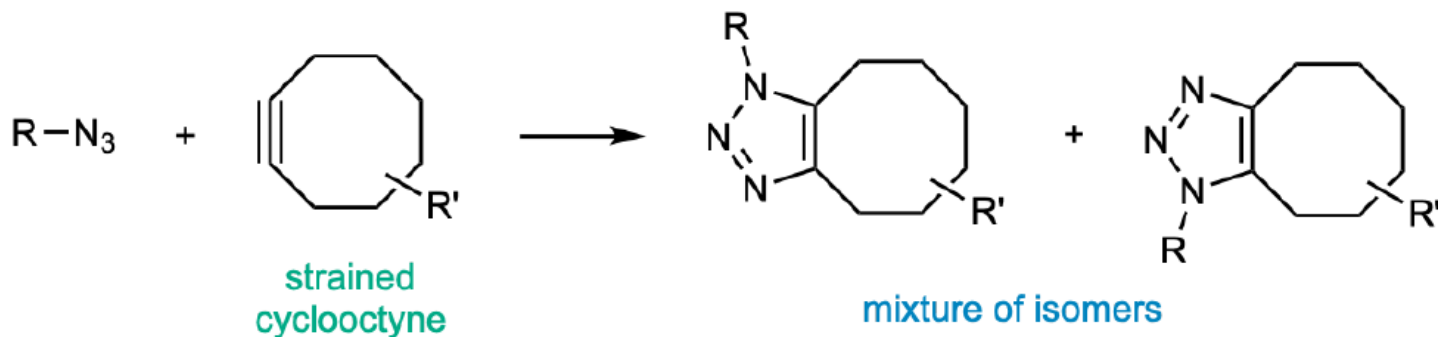
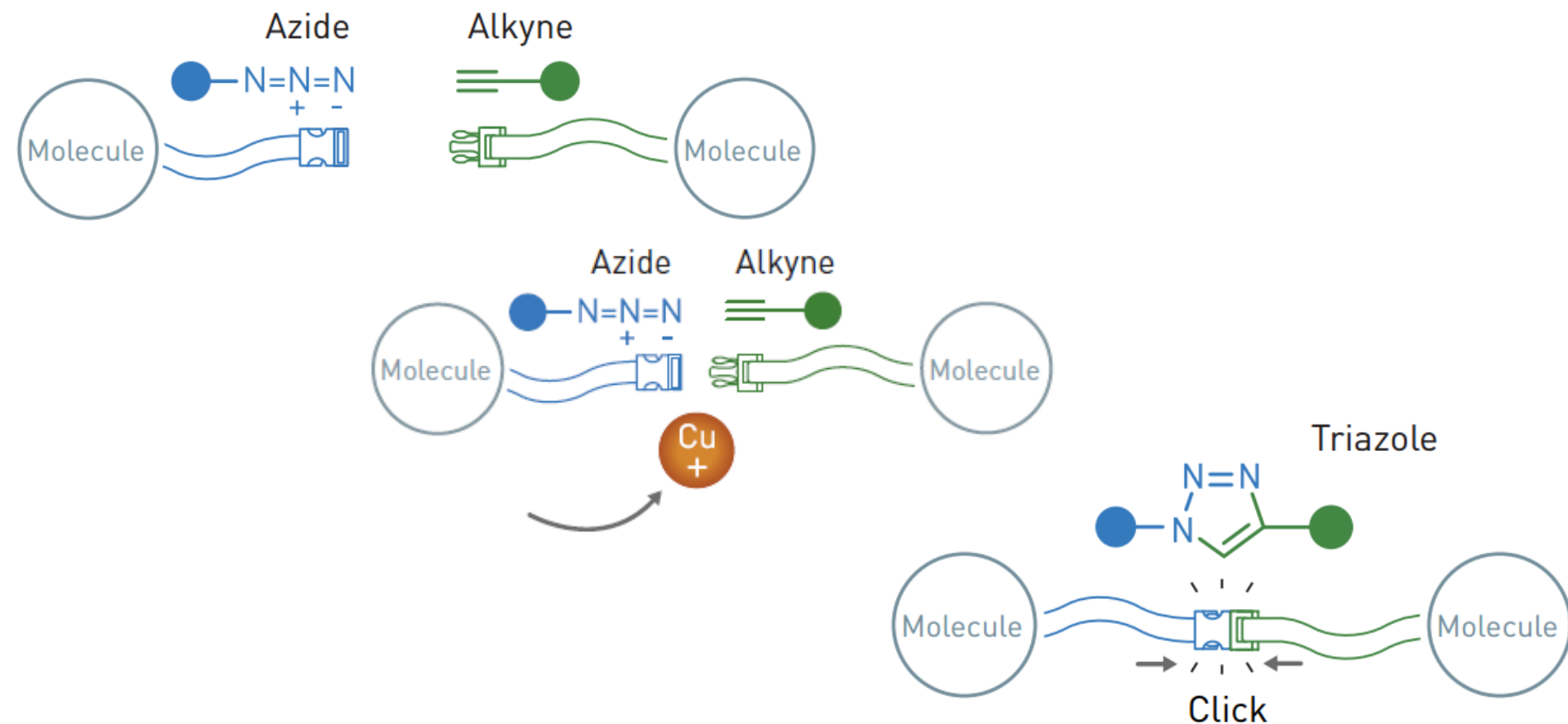
[3+2] 1,3- Dipolar Cycloadditions
Norbornene/Alkyne + **Phenyl Azide**



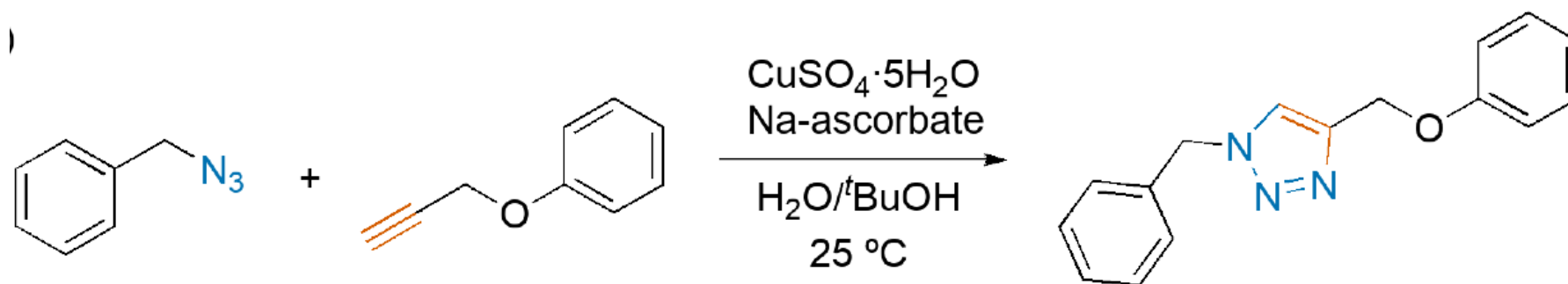
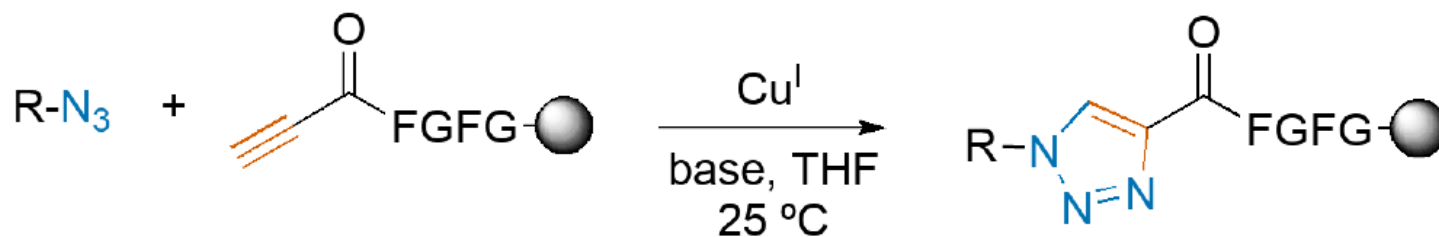
Azide-Alkyne Cycloaddition



Cu(I)- or Strain-promoted Azide-Alkyne Cycloaddition



Cu(I)-catalyzed Azide-Alkyne Cycloaddition (2001-2002)



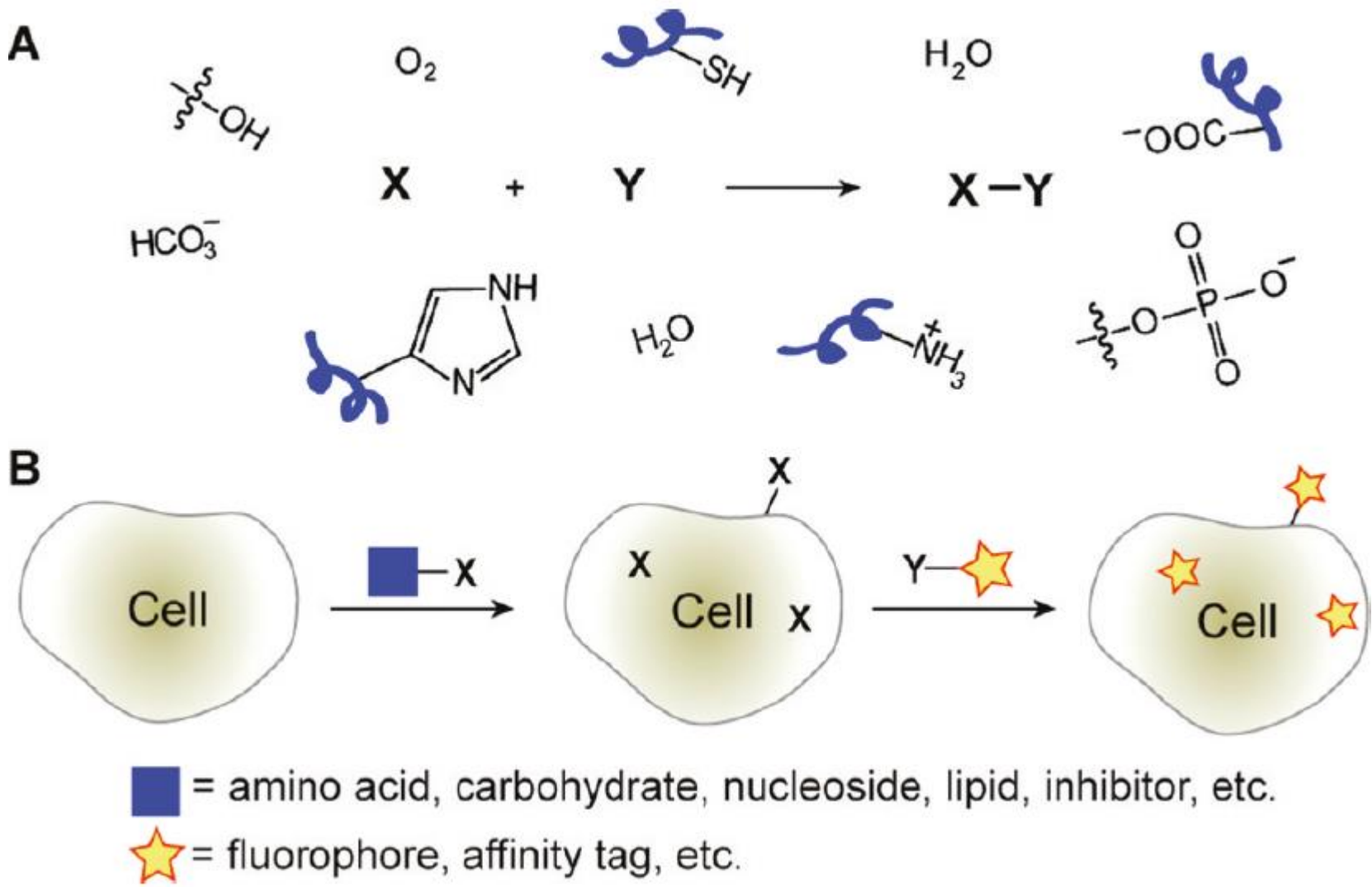
or no success. L'abbé reported the in situ generation of a propargyl azide by displacement of a sulfonate with lithium azide and copper(I) chloride.¹⁴ Instead of the expected product, an alkyl-substituted [1,2,3]-triazole byproduct was isolated in low yield. This side reaction was not investigated further. One communication with limited scope and experimental details described the solid-phase synthesis of [1,2,3]-triazoles by a diazo transfer reaction with tosyl azide.¹⁵ The present investigations

(14) L'abbé, G. *Bull. Soc. Chim. Belg.* **1984**, 93, 579–592.

(15) Zaragoza, F.; Petersen, S. V. *Tetrahedron* **1996**, 52, 10823–10826.

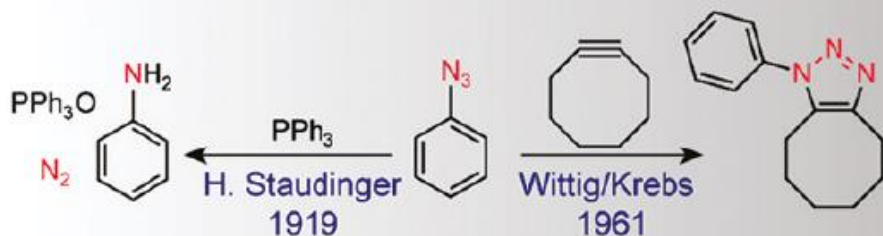
Bioorthogonal reactions

“...reactions of functional groups that are so **selective** for each other that they can be ligated in a richly functionalized biological milieu.

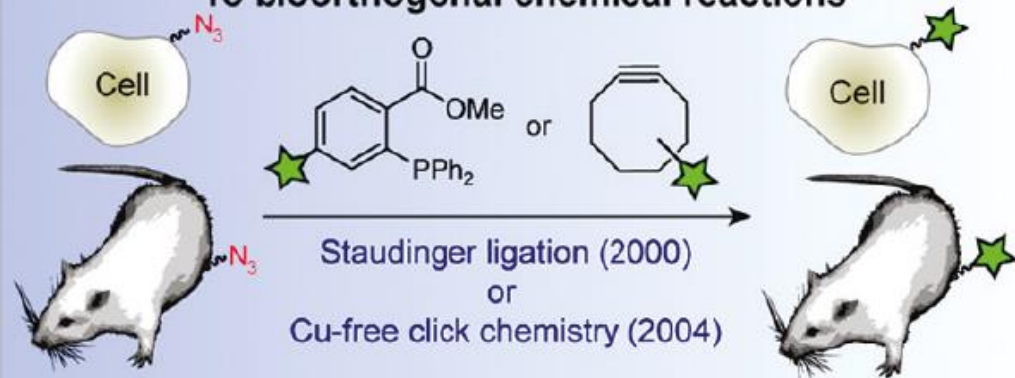


Staudinger reaction (Nobel Prize in Chemistry 1953)

From classic organic chemistry



To bioorthogonal chemical reactions



Staudinger reaction in biology (2000)

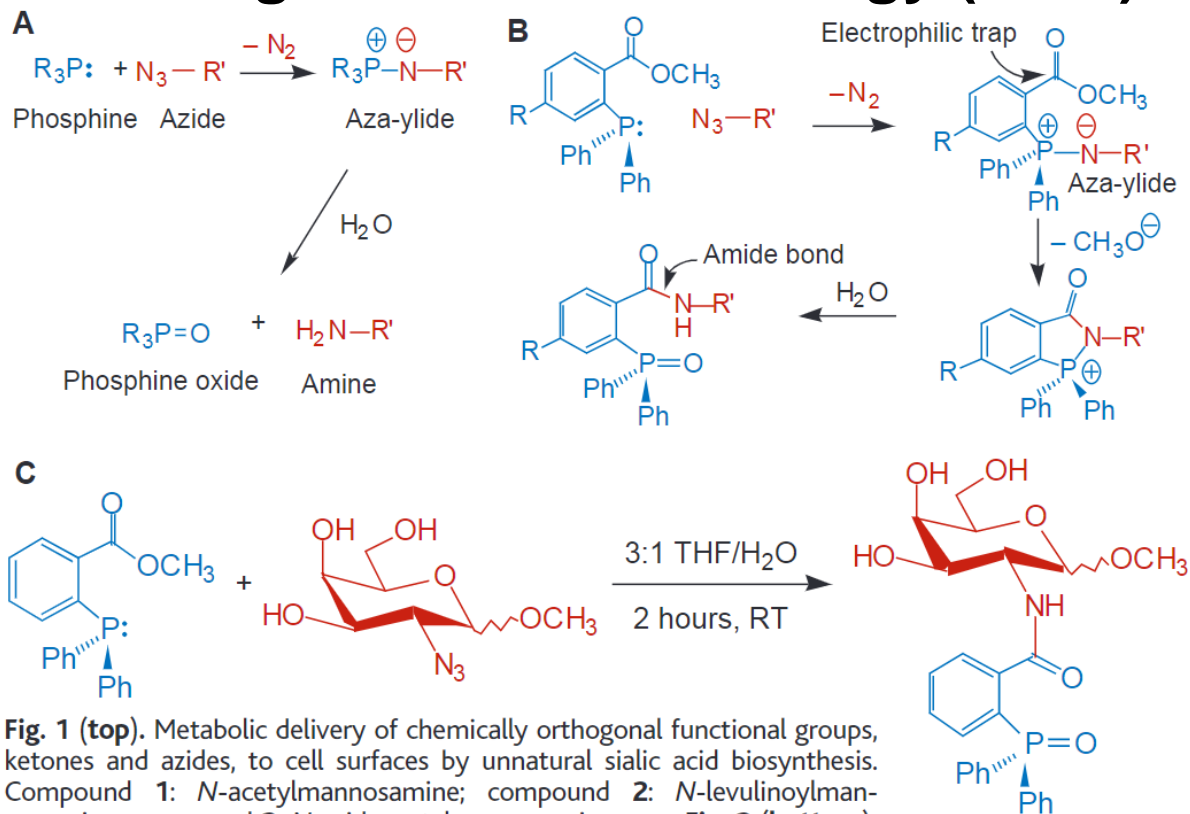
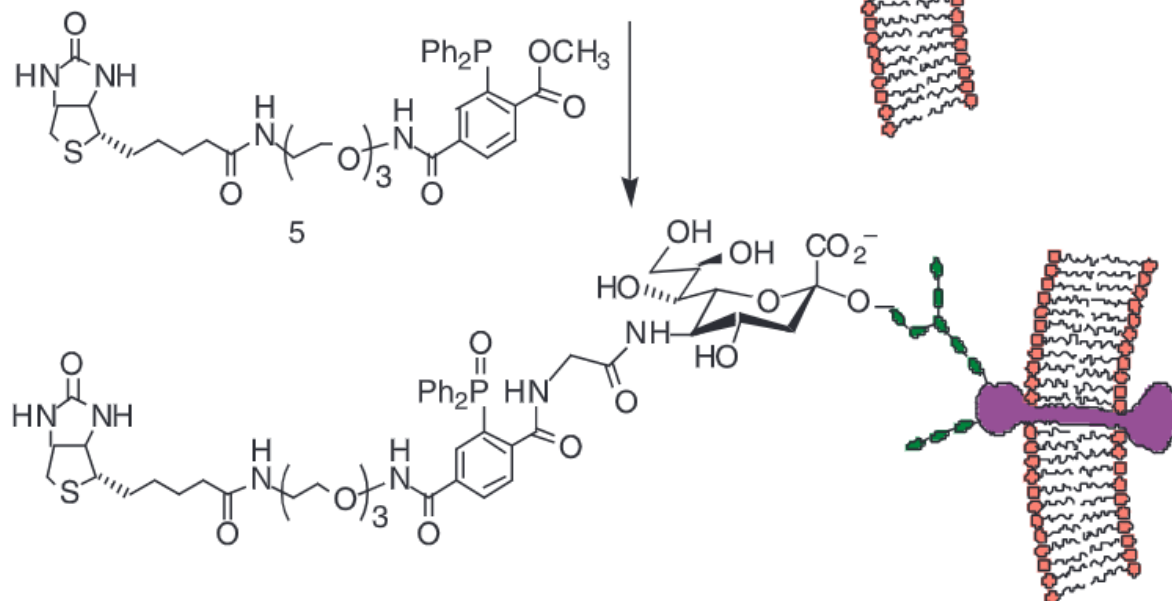
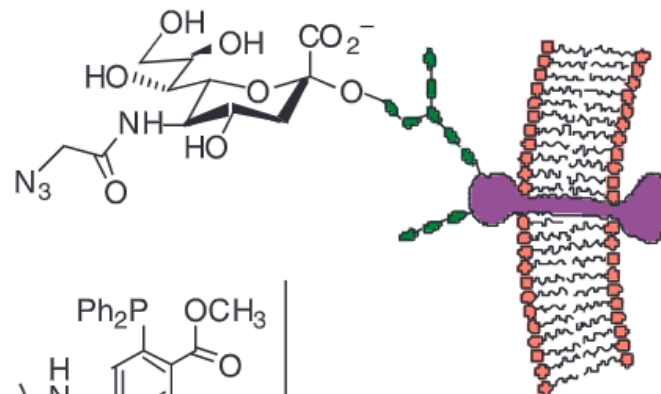
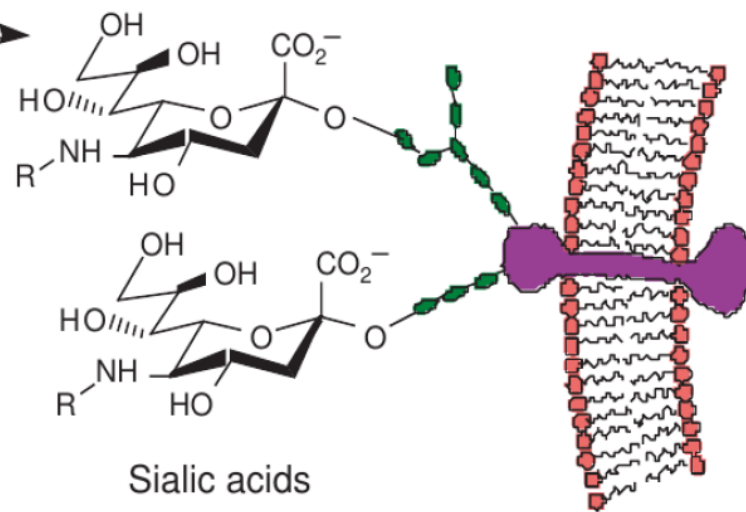
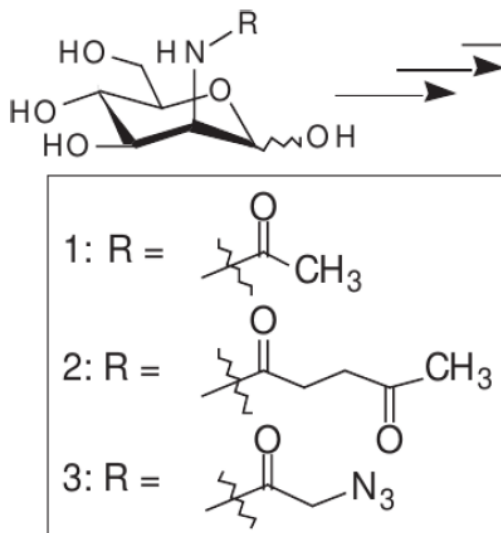


Fig. 1 (top). Metabolic delivery of chemically orthogonal functional groups, ketones and azides, to cell surfaces by unnatural sialic acid biosynthesis. Compound 1: *N*-acetylmannosamine; compound 2: *N*-levulinoylman-

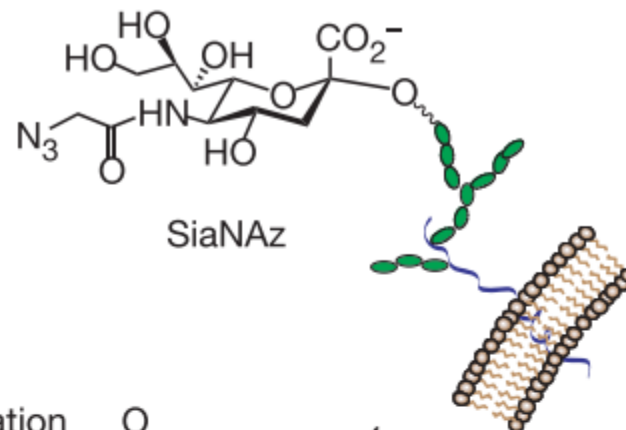
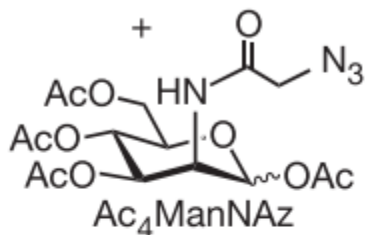


Staudinger reaction in live animal (2004)

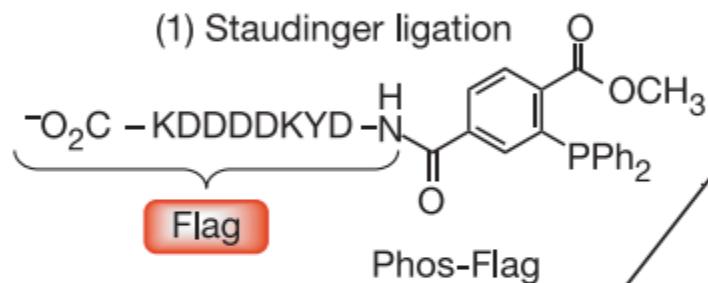


(1) Inject Ac_4ManNAz solution for 7 days

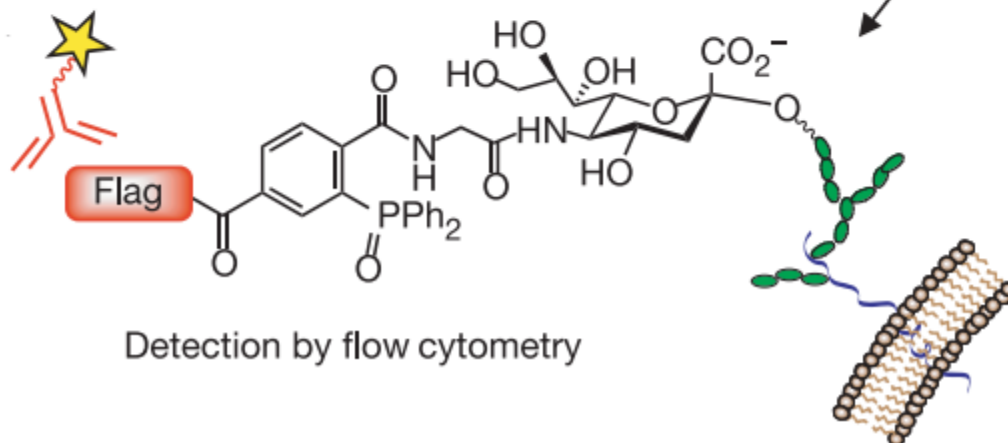
(2) Isolate splenocytes



(1) Staudinger ligation

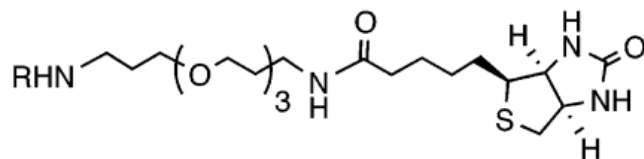
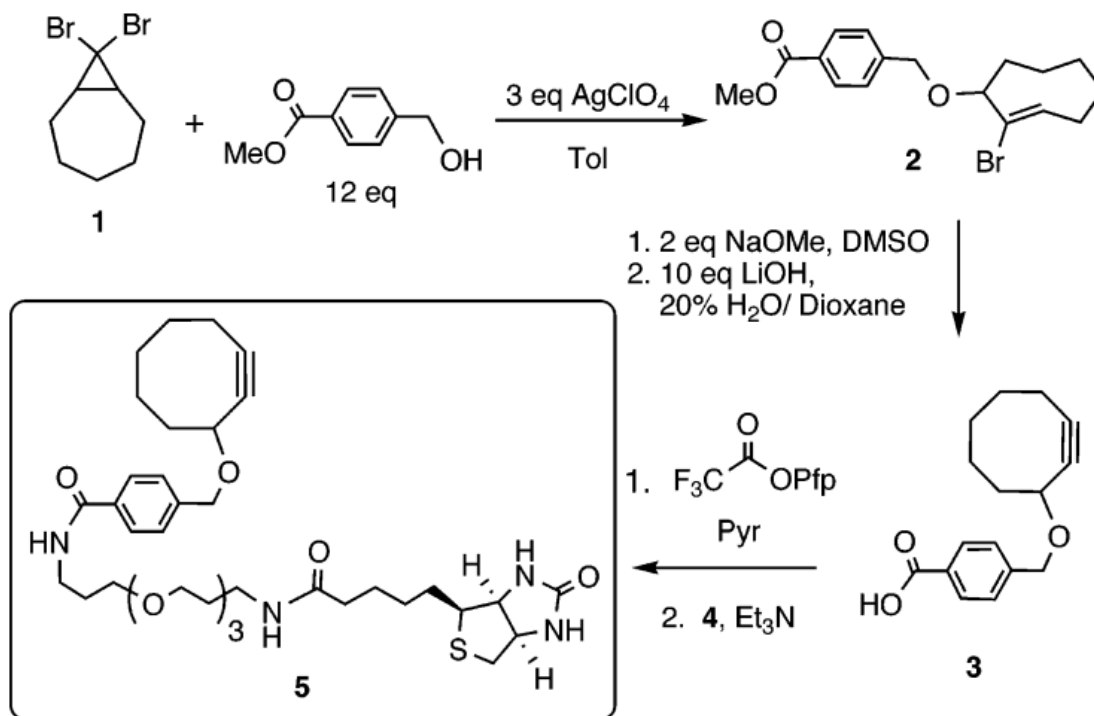
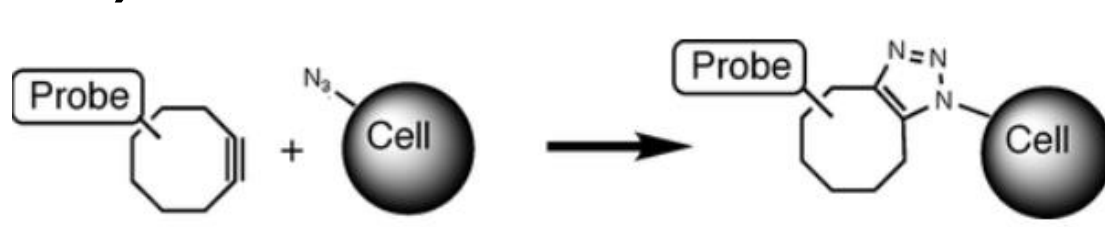


(2) FITC-anti-Flag



Detection by flow cytometry

Strain-promoted Azide-Alkyne Cycloaddition in Living Systems (2004)



4 R = H

6 R =

