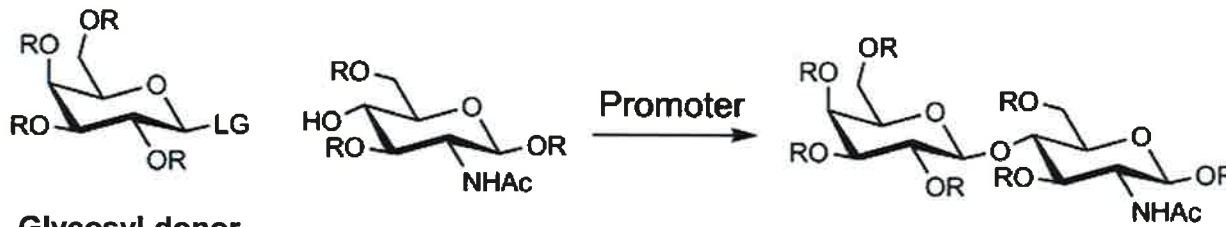


Carbohydrate Synthesis – The chemists toolbox

Control: Chemo-, regio-, and stereoselectivity

Chemical vs. enzymatic glycosylation

Chemical



Glycosyl donor

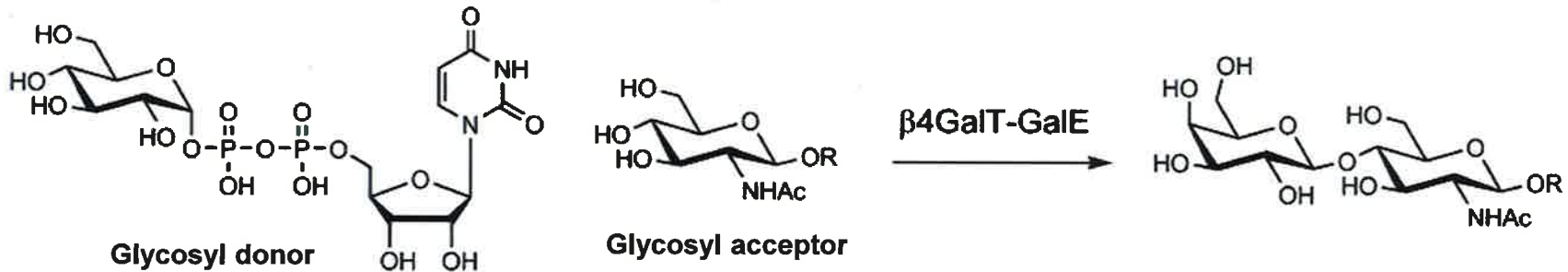
2-3 steps from
free sugars

Glycosyl acceptor

6-8 steps from free
sugars

Deprotection

Enzymatic



Glycosyl donor

Glycosyl acceptor

Glycosyltransferases

Biosynthesis of oligosaccharides

Formation of defined stereo- and regiospecific products

Leloir enzymes - utilize activated glycosyl esters of nucleoside mono- or diphosphates as glycosyl donors (Luis F. Leloir)

Advantages:

Formation of defined products

No protecting group chemistry

Mild conditions (room temperature, aqueous conditions)

Limitations for synthesis:

Substrate specificity

High cost of glycosyl nucleotide donor

Limited enzyme availability

Enzyme activity: moles of substrate converted per unit time

$$1 \text{ enzyme unit (U)} = 1 \mu\text{mol min}^{-1}$$

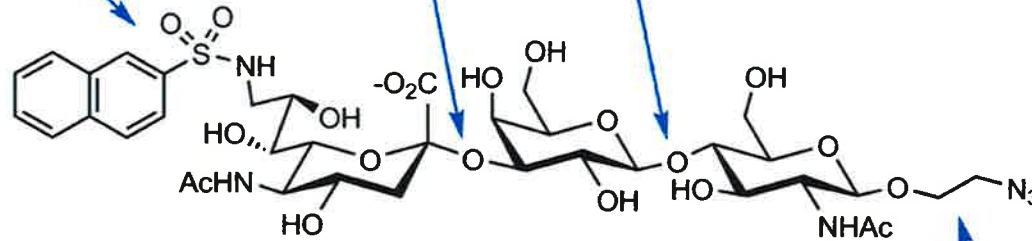
Carbohydrate Synthesis

Chemo-enzymatic synthesis

Combination of both chemical and enzymatic methods

Functional group
modifications
(chemical)

Glycosylations
(enzymatic)



Where to start?

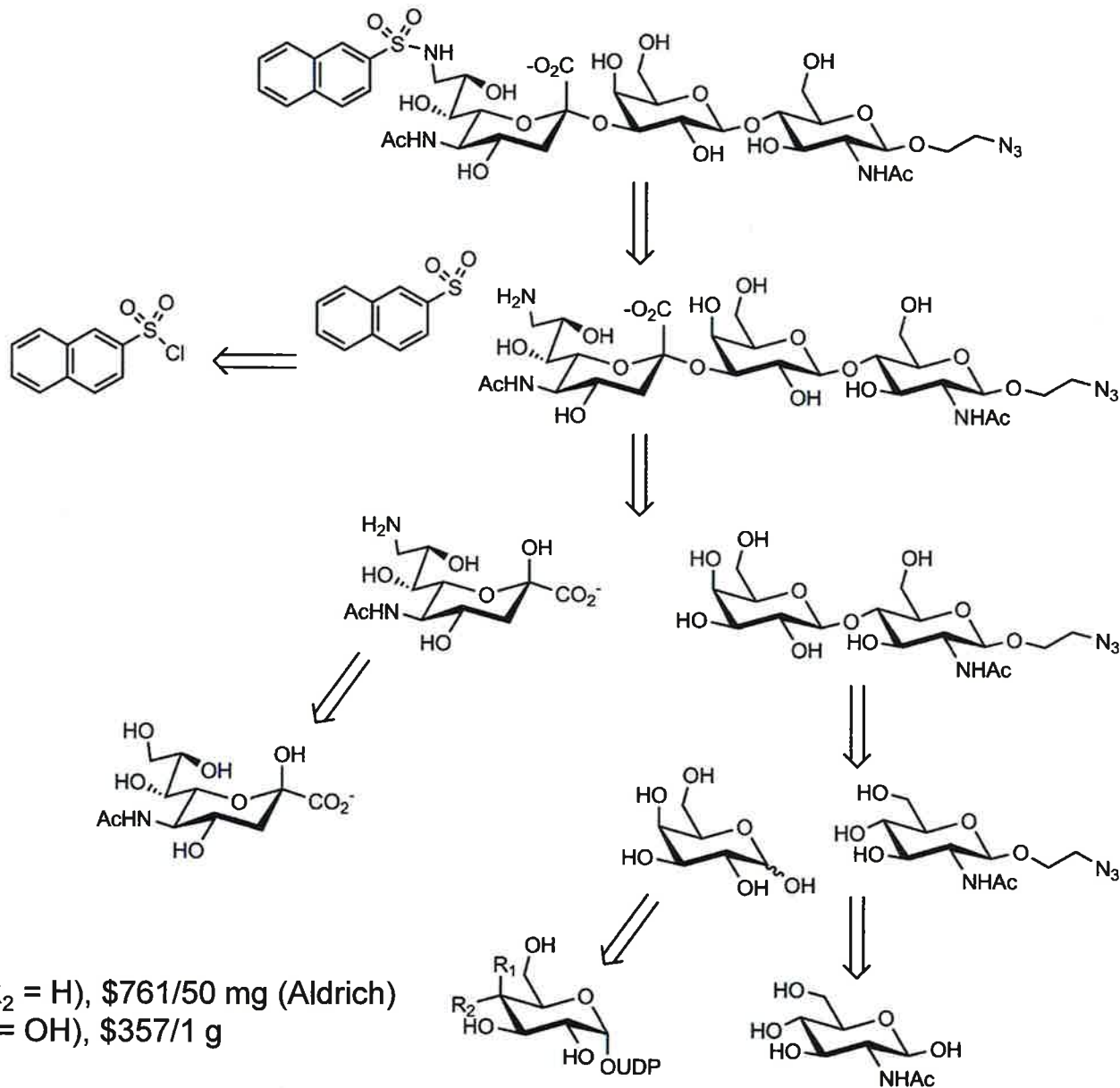
Installation of aglycone
(chemical)

Retro-Synthetic analysis of glycan structure

Technique for solving problems in the planning of organic syntheses
(E.J. Corey, Harvard)

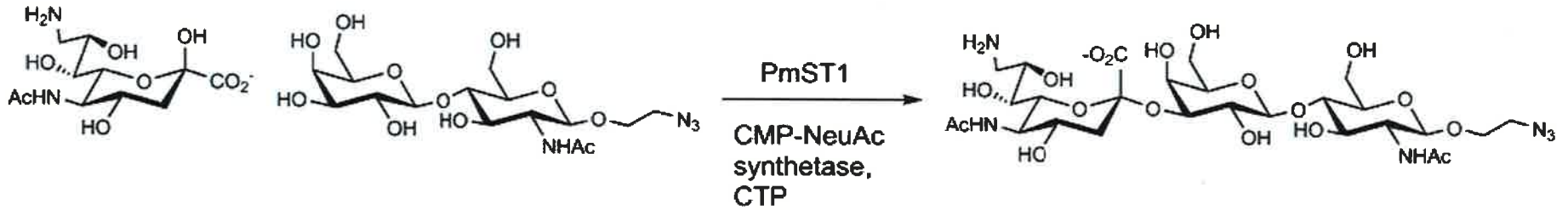
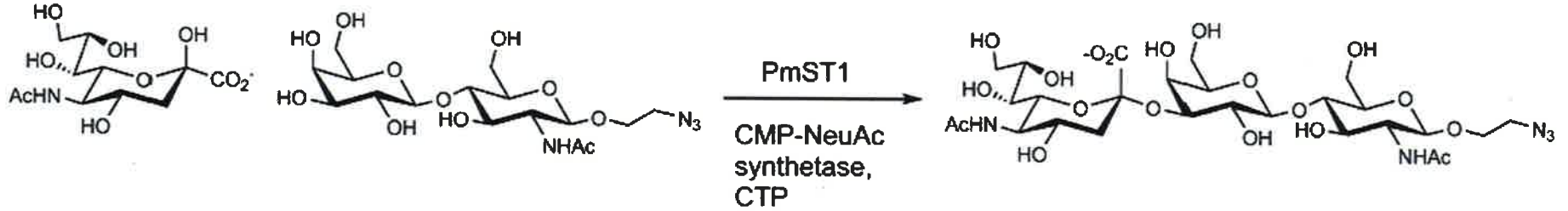
Aim: Structural simplification through bond disconnection

Identify key building blocks (ideally commercially available)

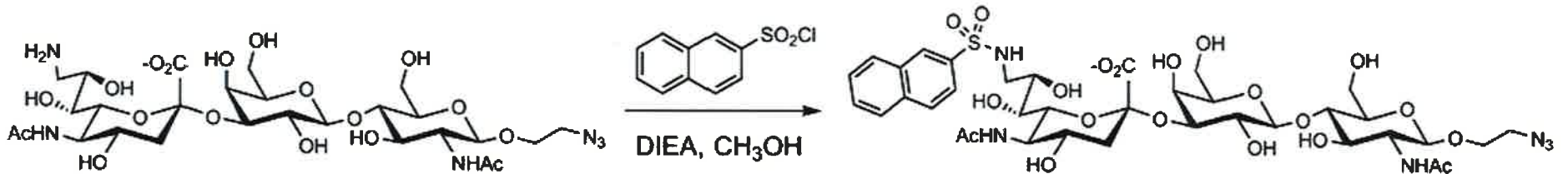


Module 1 - Reactions

1. Sialylations:

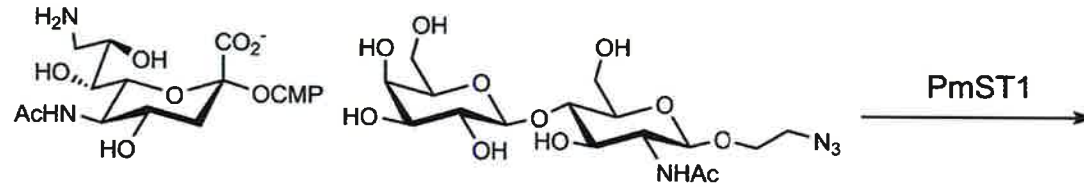


2. Sulfonamide synthesis

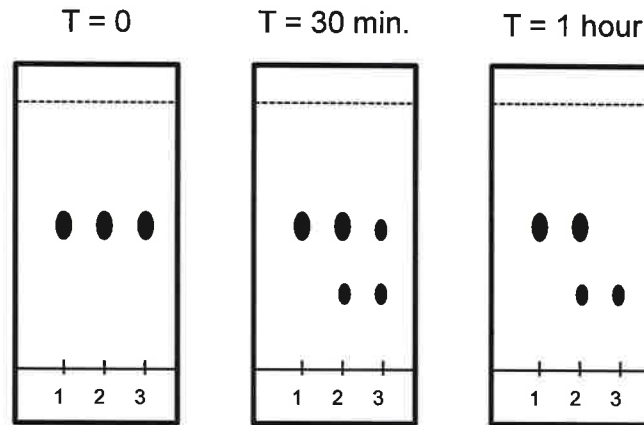


Reaction steps

1. Setup



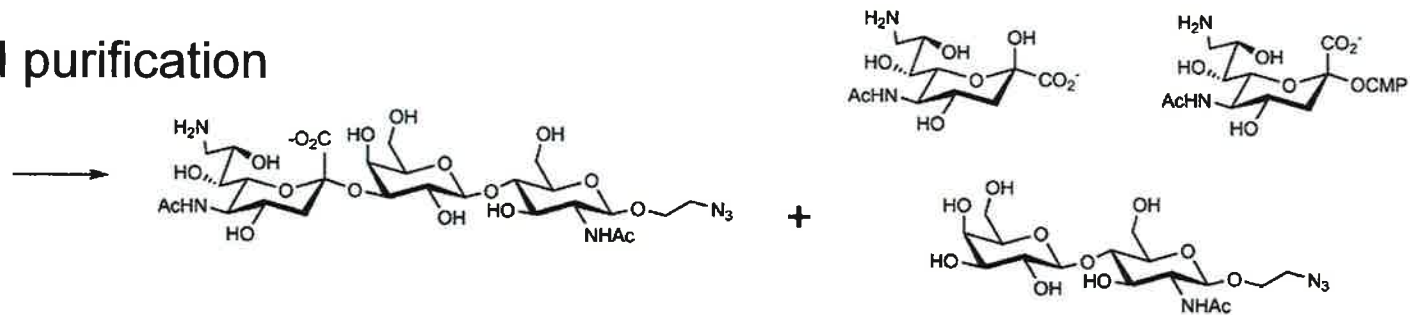
2. Monitor



Thin layer chromatography

1. Starting material
2. Co-spot
3. reaction

3. Work-up and purification



CMP, CTP
Enzymes
Buffer salts