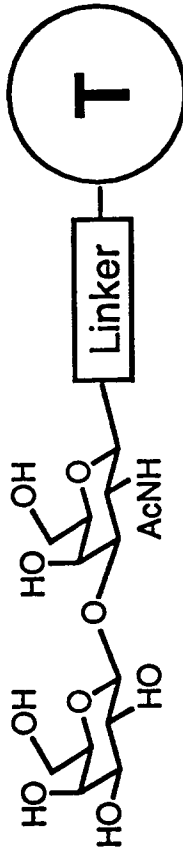
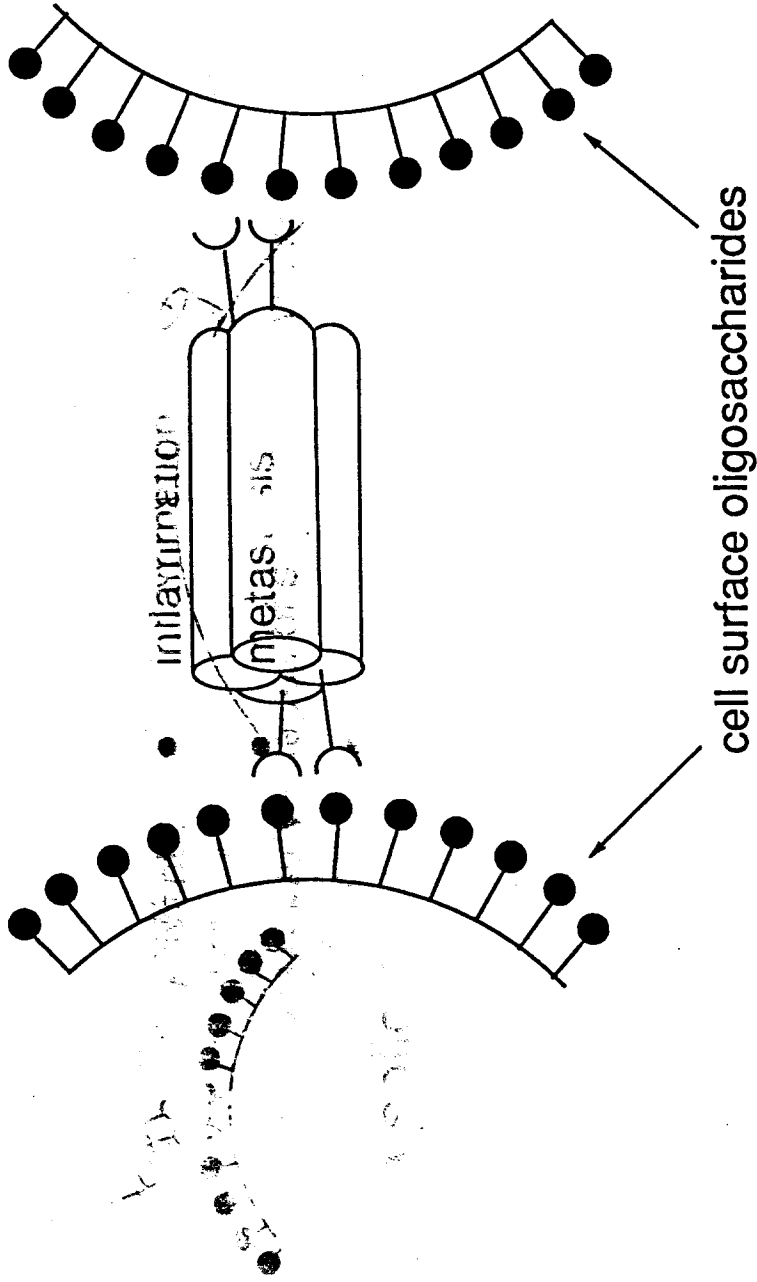


The First Solid Phase Carbohydrate Library

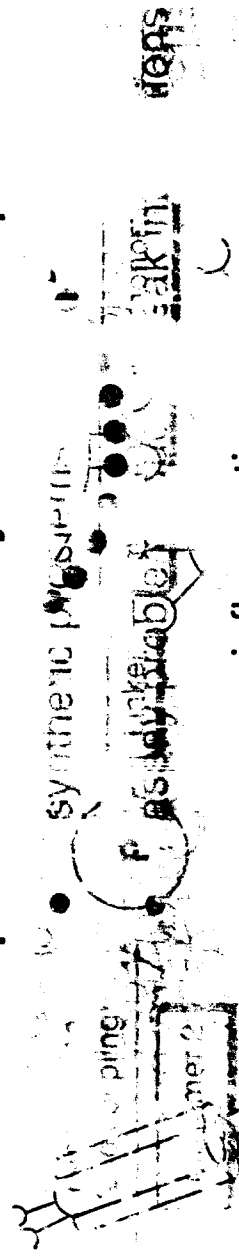


The target of the library:

a carbohydrate binding protein that promotes cell adhesion

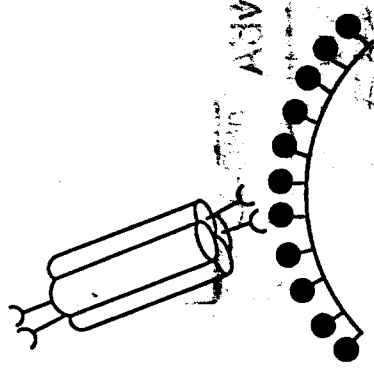
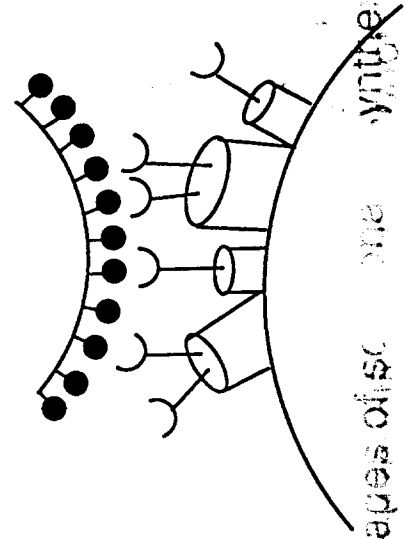
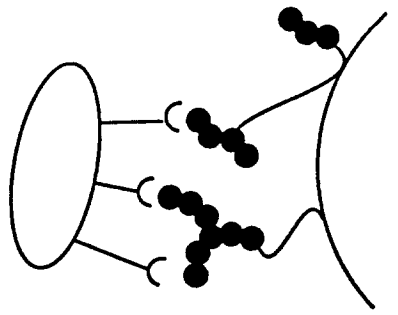


Carbohydrate-protein interactions are important in many adhesion processes:



- inflammation
- metastasis
- viral infection
- bacterial infection

Adhesion involves polyvalent contacts:



Advantages

Advantages of disc

A solid

Adhesion is strong...
but the individual contacts are weak

Carbohydrates involved in adhesion processes have been difficult to study for two reasons:

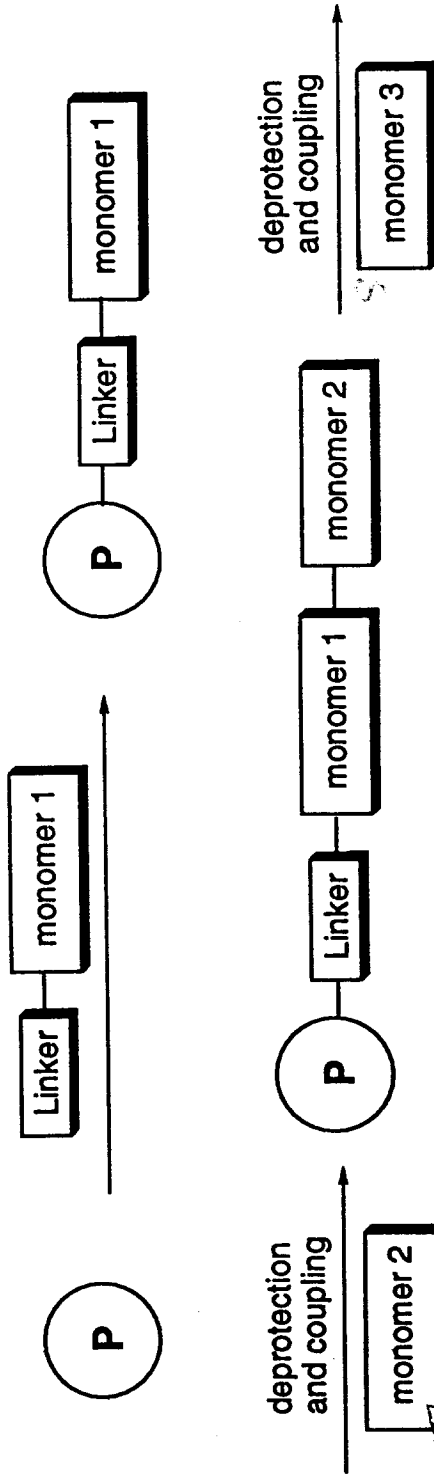
• synthetic problems

• assay problems due to weak interactions

A solid phase carbohydrate library could solve both problems.

The key to s

Solid Phase Synthesis



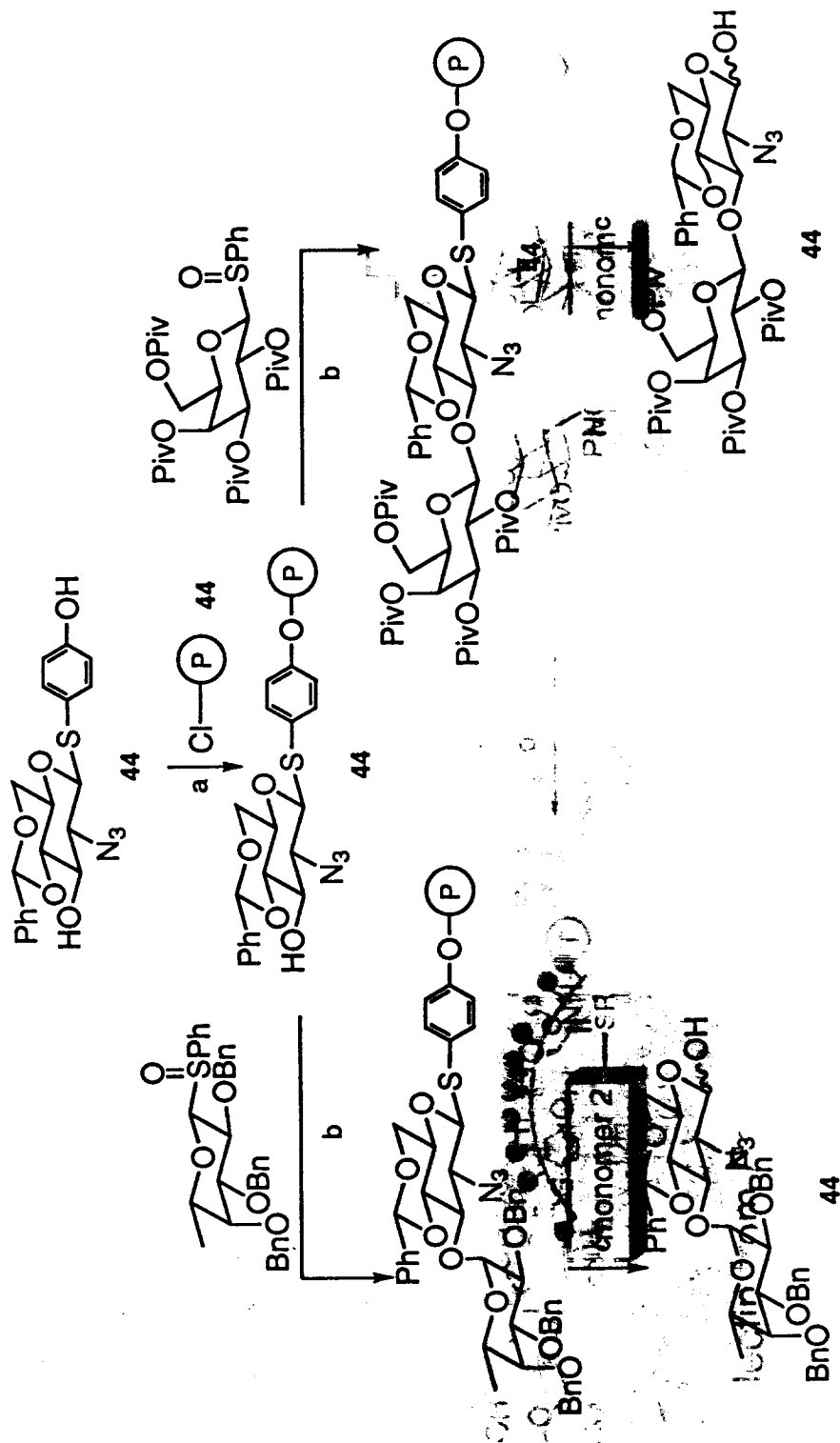
Advantages:

Advantages of solid phase synthesis:

- fast
- high yields
- spatial resolution

The key to solid phase synthesis is a good method for coupling monomers

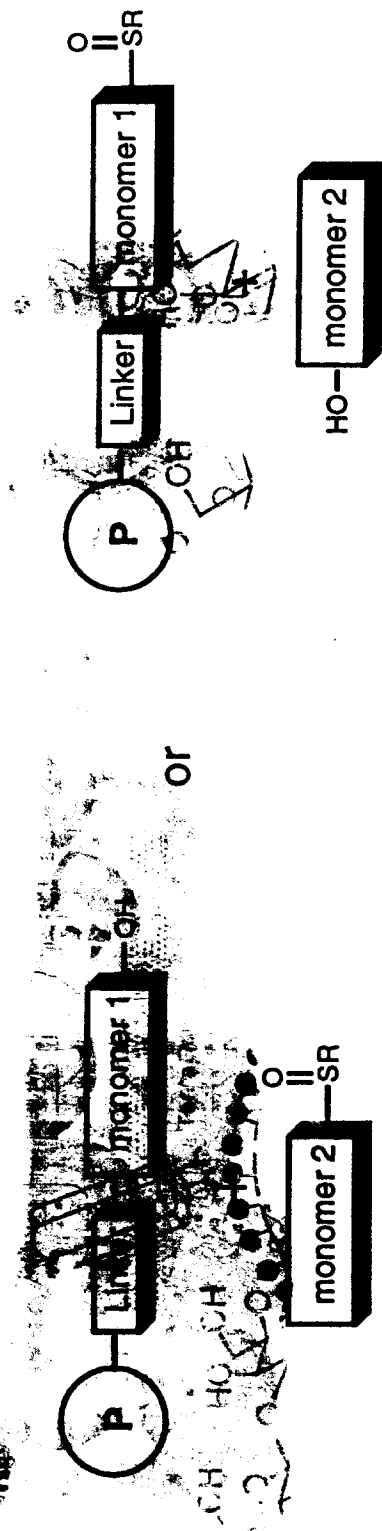
Stereoselective glycosylation on the Merrifield resin



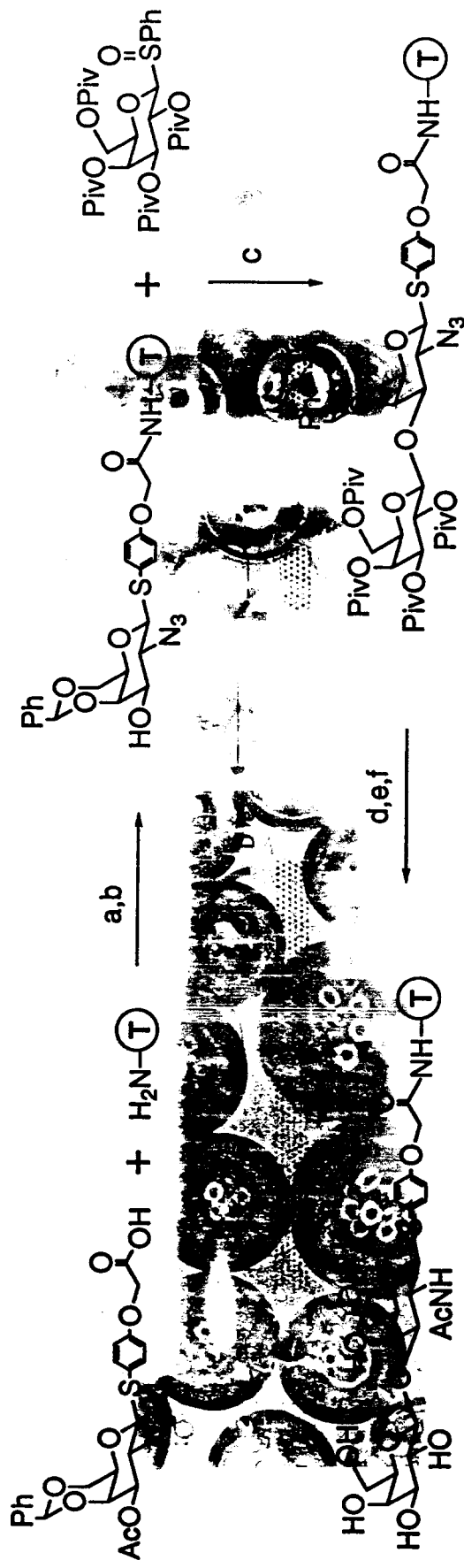
Conditions: a) Cs_2CO_3 , N-methylpyrrolidone, 55 °C, 8 h; b) TiF_2O , DTBMP, CH_2Cl_2 , -60 to -30 °C, 2 h; c) $\text{Hg}(\text{OCCOCF}_3)_2$, wet CH_2Cl_2 , 2 h.

Strategic Issues in Carbohydrate Library Synthesis

- support: soluble or insoluble?
- direction of synthesis: reducing to non-reducing or vice versa?

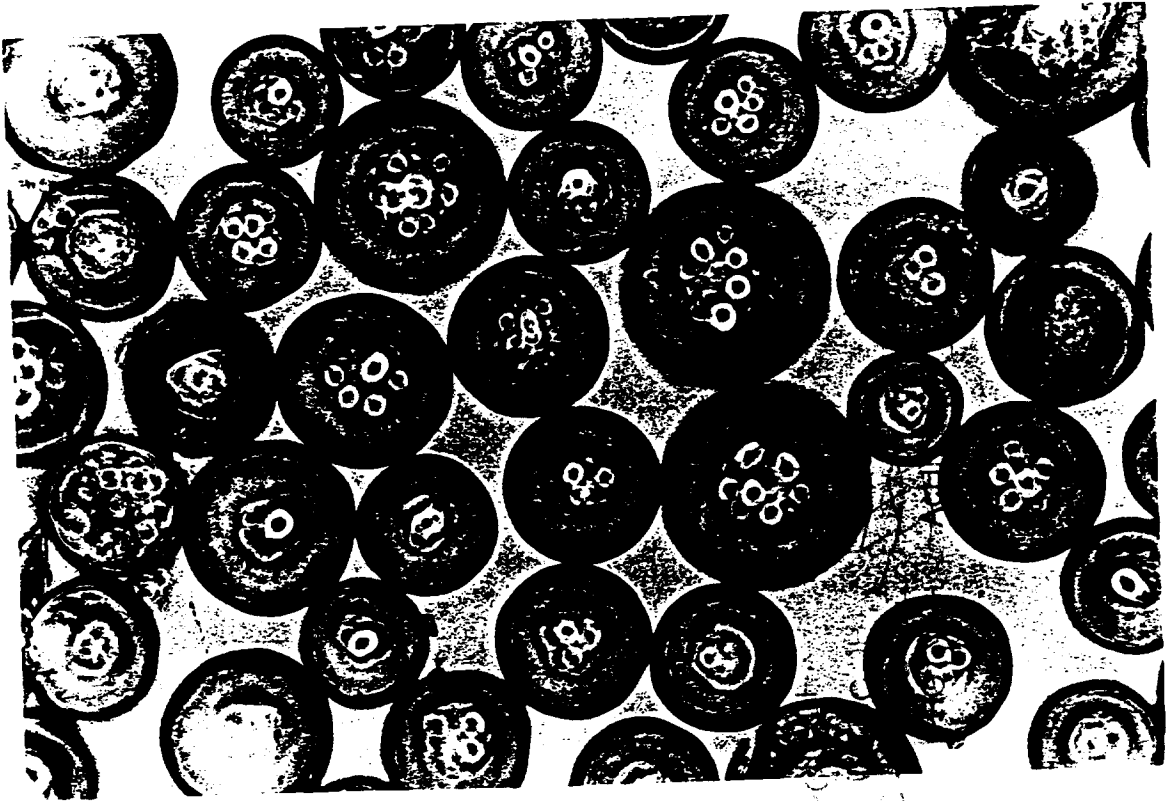
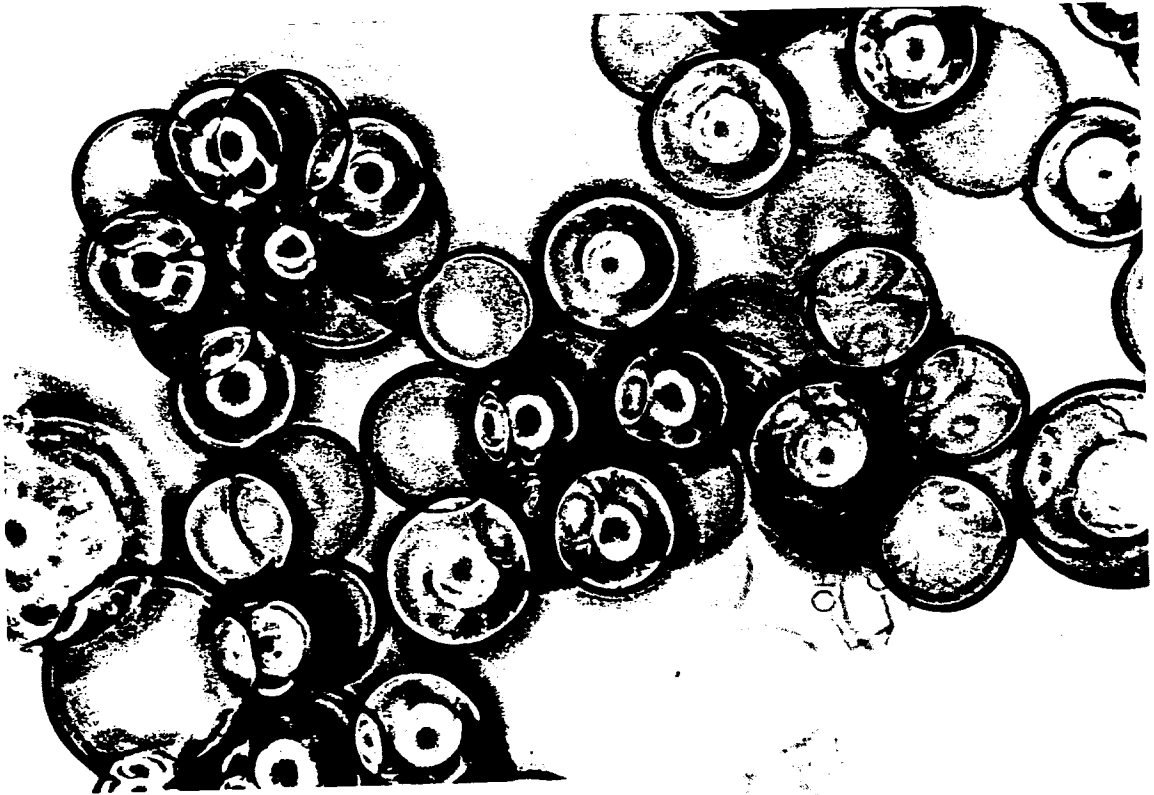


- glycosylation method?

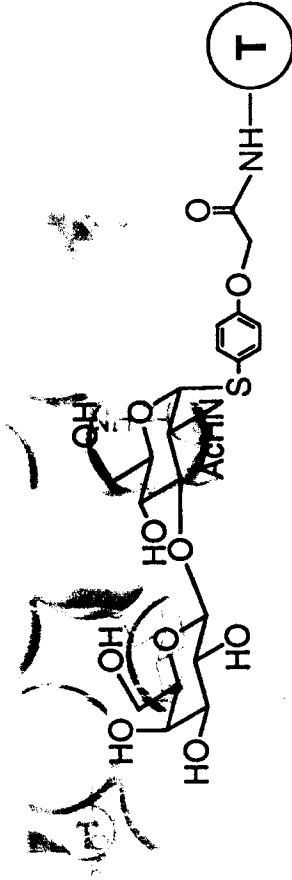
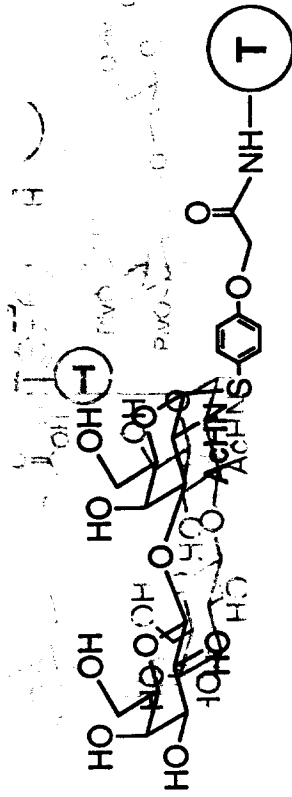
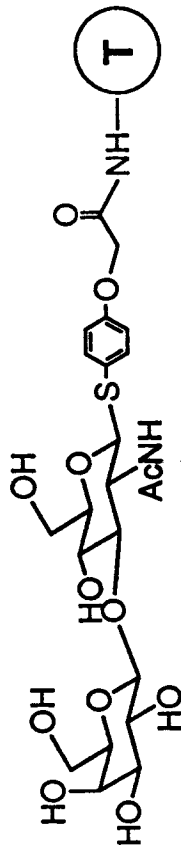
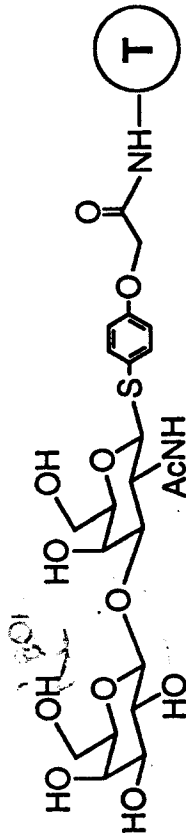


Synthesis of Galβ(1-3)GalNAc on TentaGel

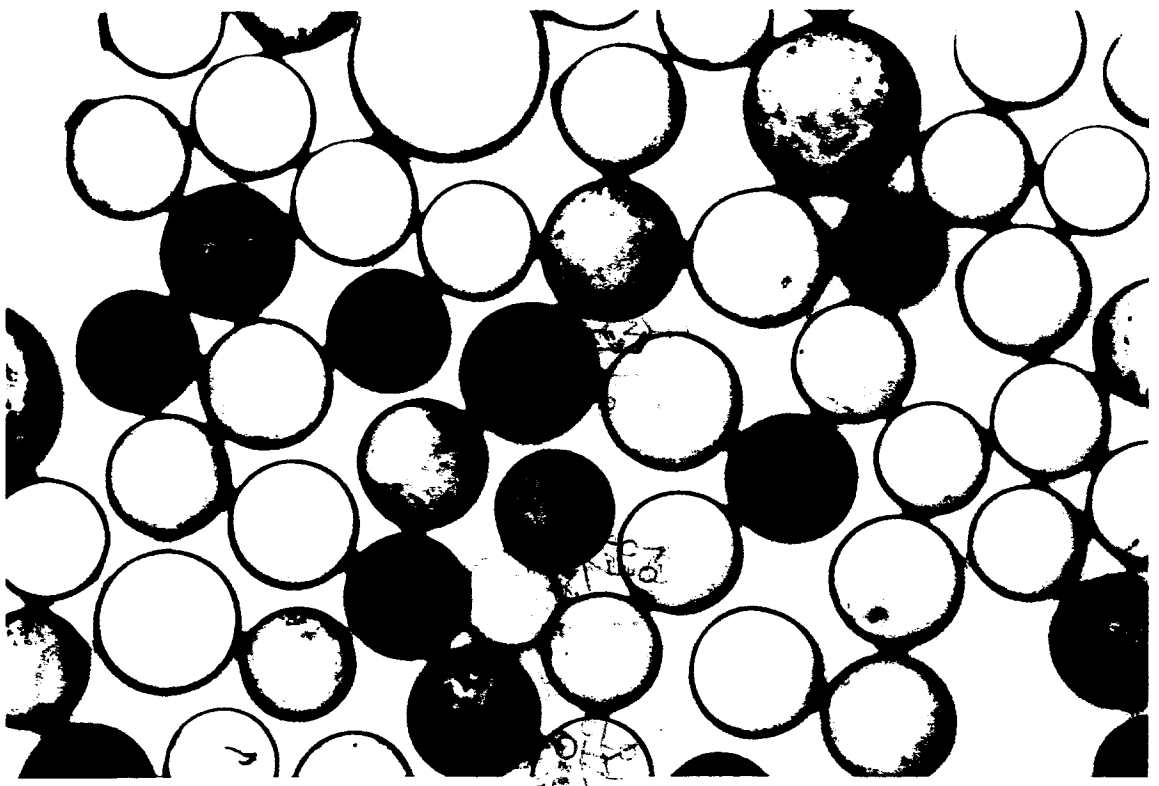
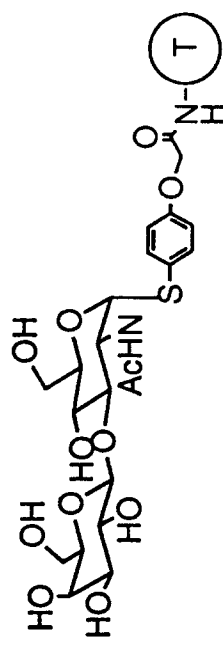
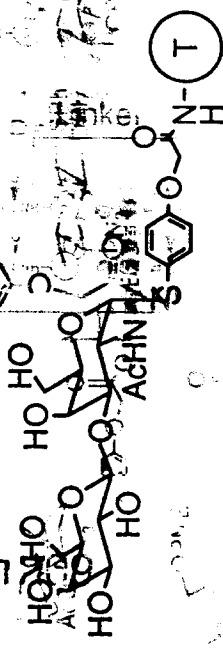
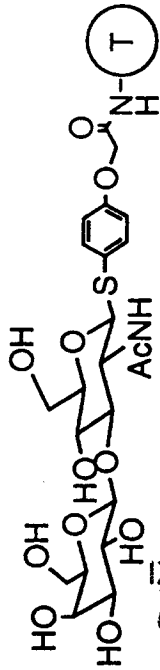
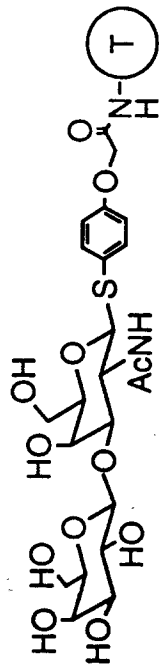
(a) HOBt/HBTU, DIEA, NMP, rt, 2 h; (b) Hydrazine/DMF (1:7), rt, 6 h; (c) Tf₂O, DTBMP, CH₂Cl₂, -78 → 0°C; repeat; (d) Thioacetic acid, rt, 24 h; (e) 20% TFA/CH₂Cl₂, rt, 30 min; (f) LiOH, MeOH/THF (1:4), rt, 8 h.



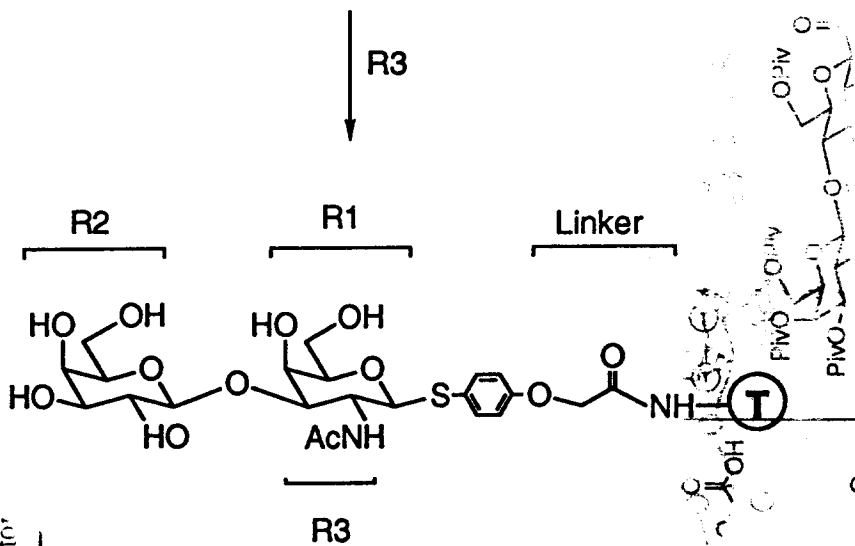
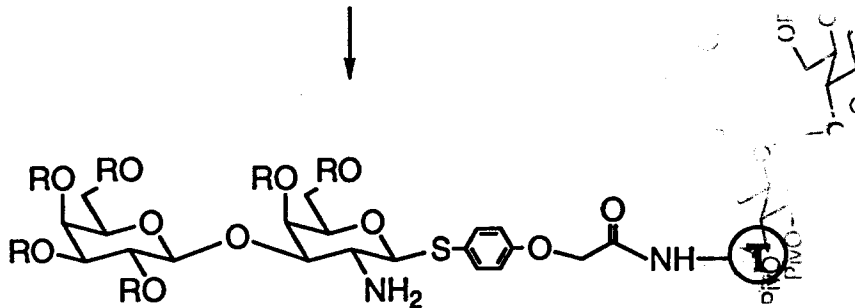
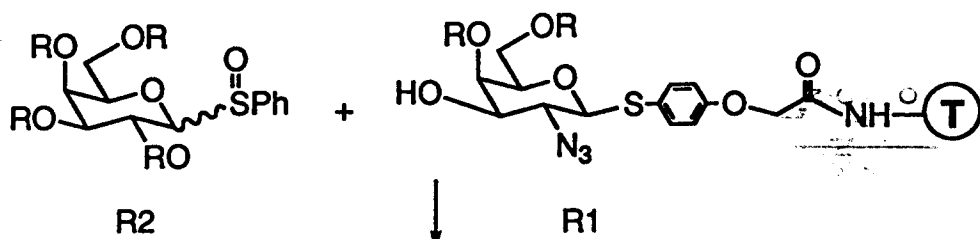
Compounds in the small library



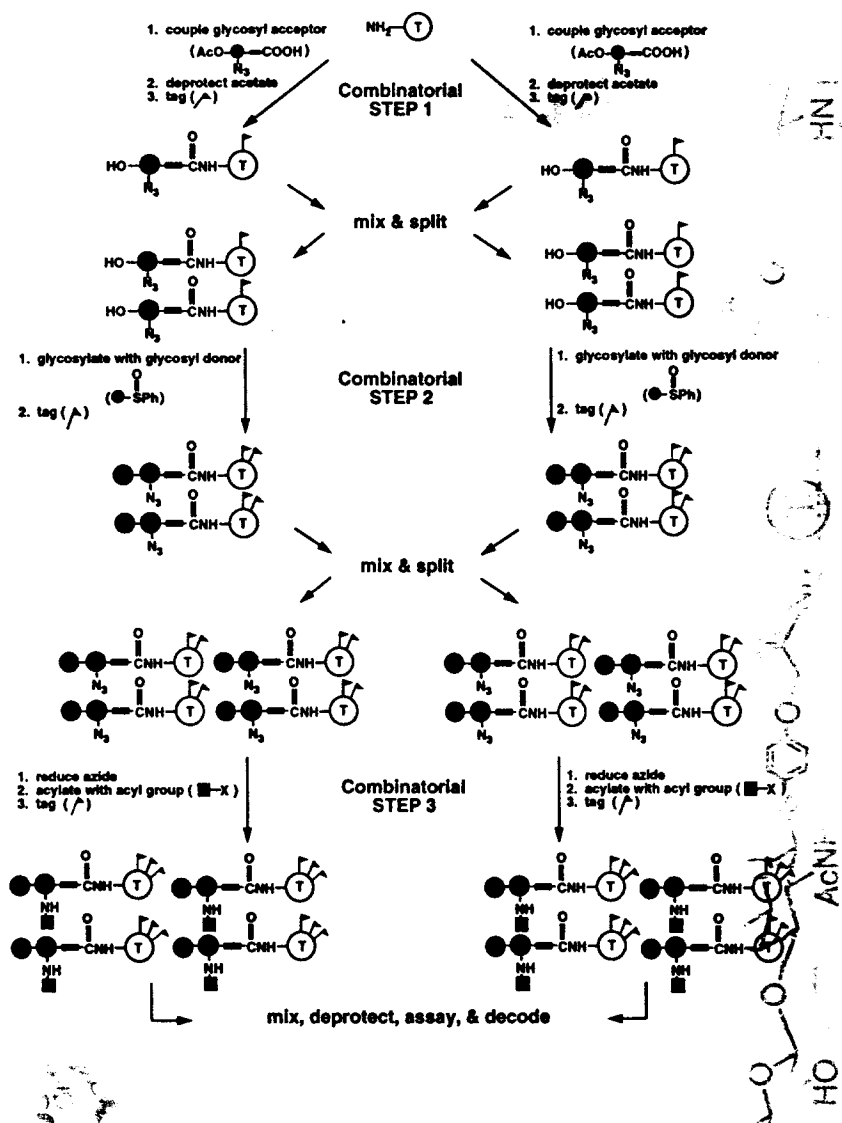
Screening of a Small Library

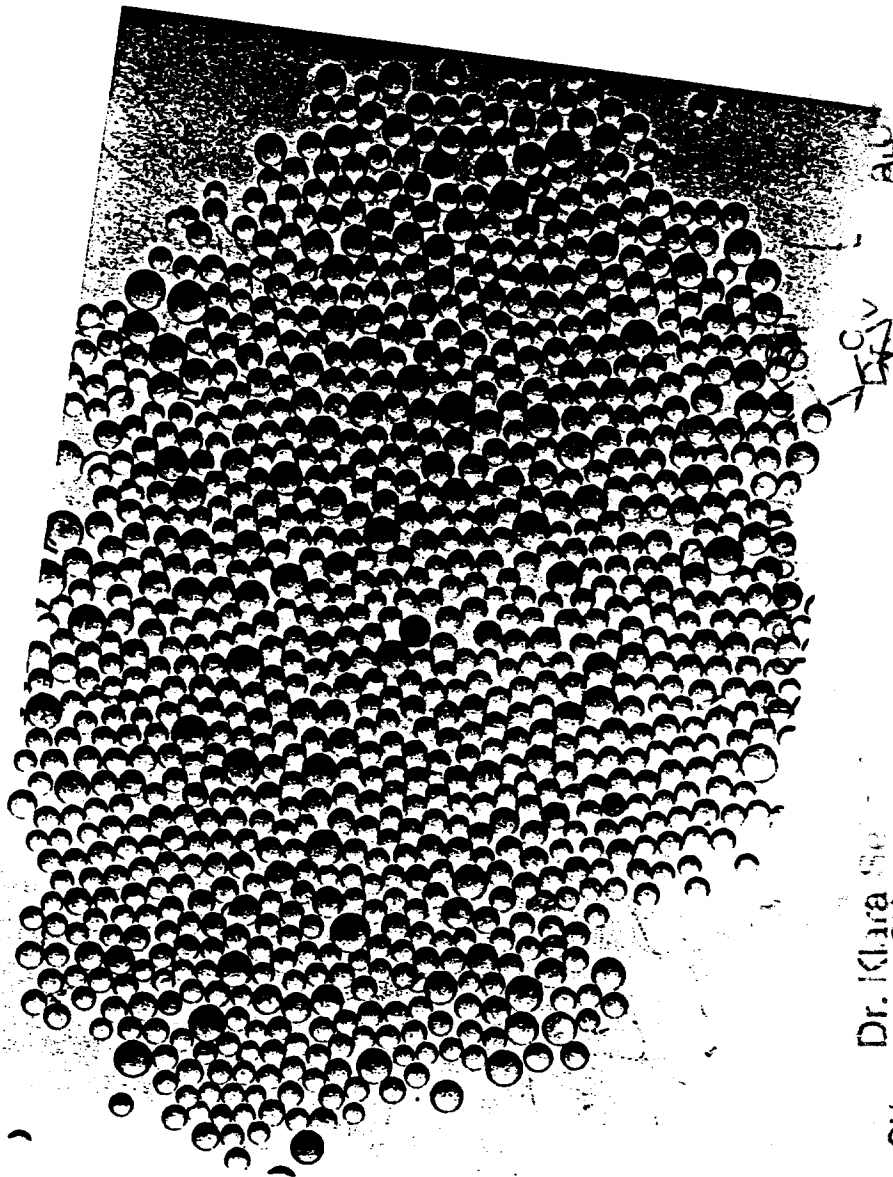


Design of the Big Library

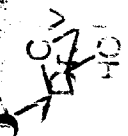


Combinatorial STEP 1 (AcO-●-COOH) N ₃ Glycosyl acceptor	Combinatorial STEP 2 (●-SPh) Glycosyl donor	Combinatorial STEP 3 (■-X) Acyl group





OH

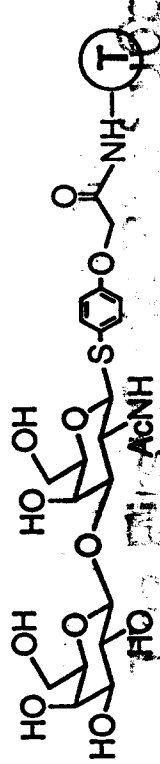


Dr. Klara Se
HO-C-OH

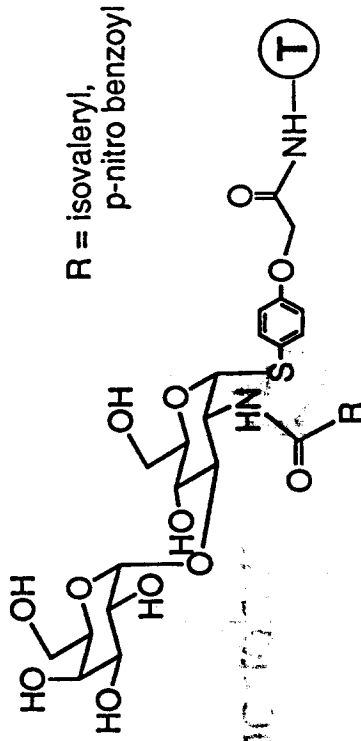


The First Solid Phase Carbohydrate Library

- the sulfonamide method is the best available glycosylation method in a library format
- spatially resolved carbohydrate libraries can provide information on structure-function relationships rapidly
- carbohydrate libraries produce unanticipated leads for carbohydrate binding proteins



natural ligand



library hit

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ONR