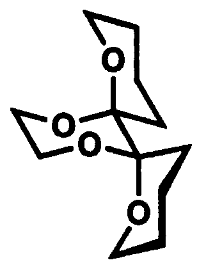
Dispiroketals in Synthesis

Vicinal diol protection

Oligosaccharide synthesis

Hydroxyacid protection



Carbohydrate chemistry

Thermodynamic resolution

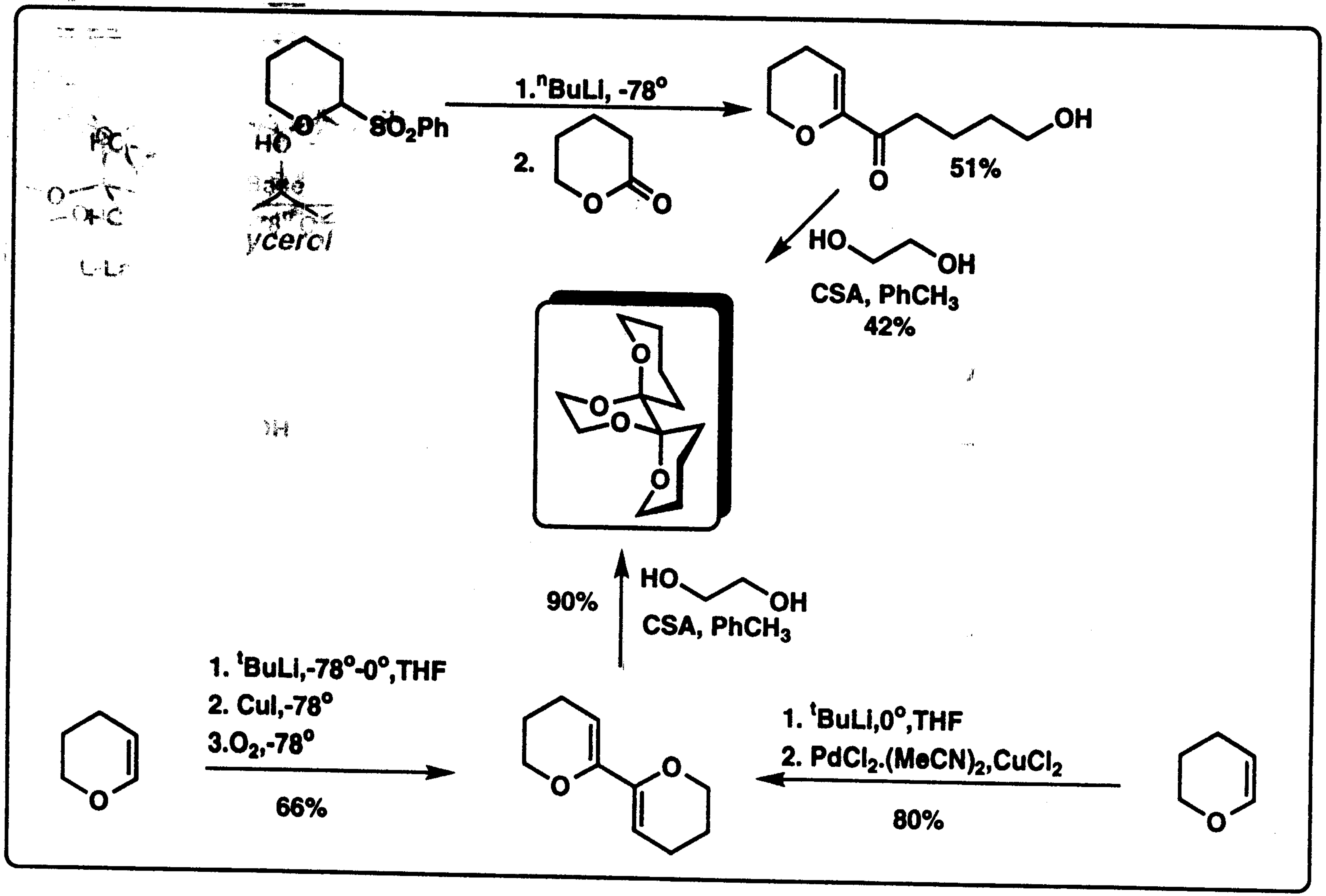
Oliosaccharide libraries

Asymmetric synthesis

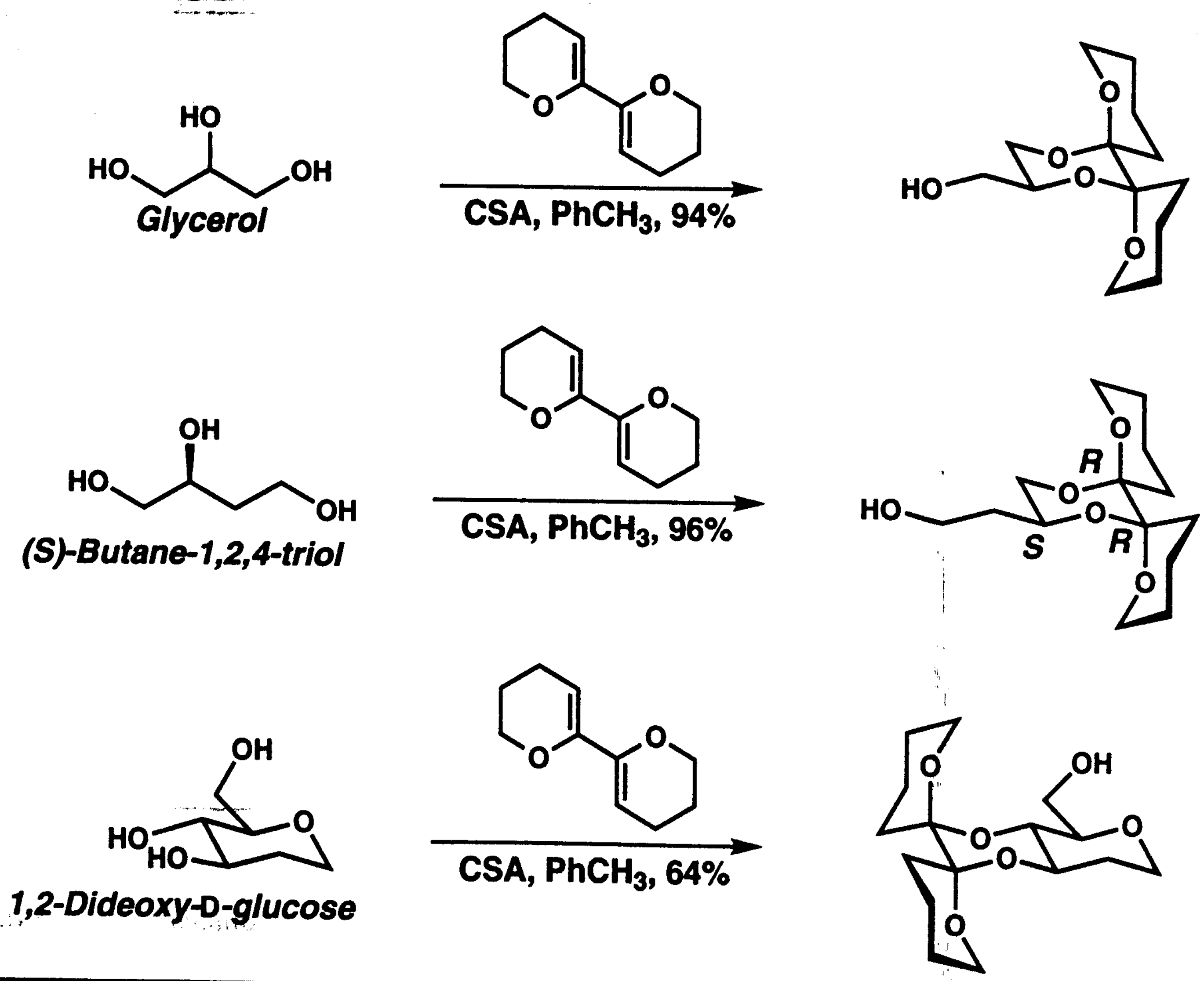
Desymmetrization reactions

Chiral auxiliaries

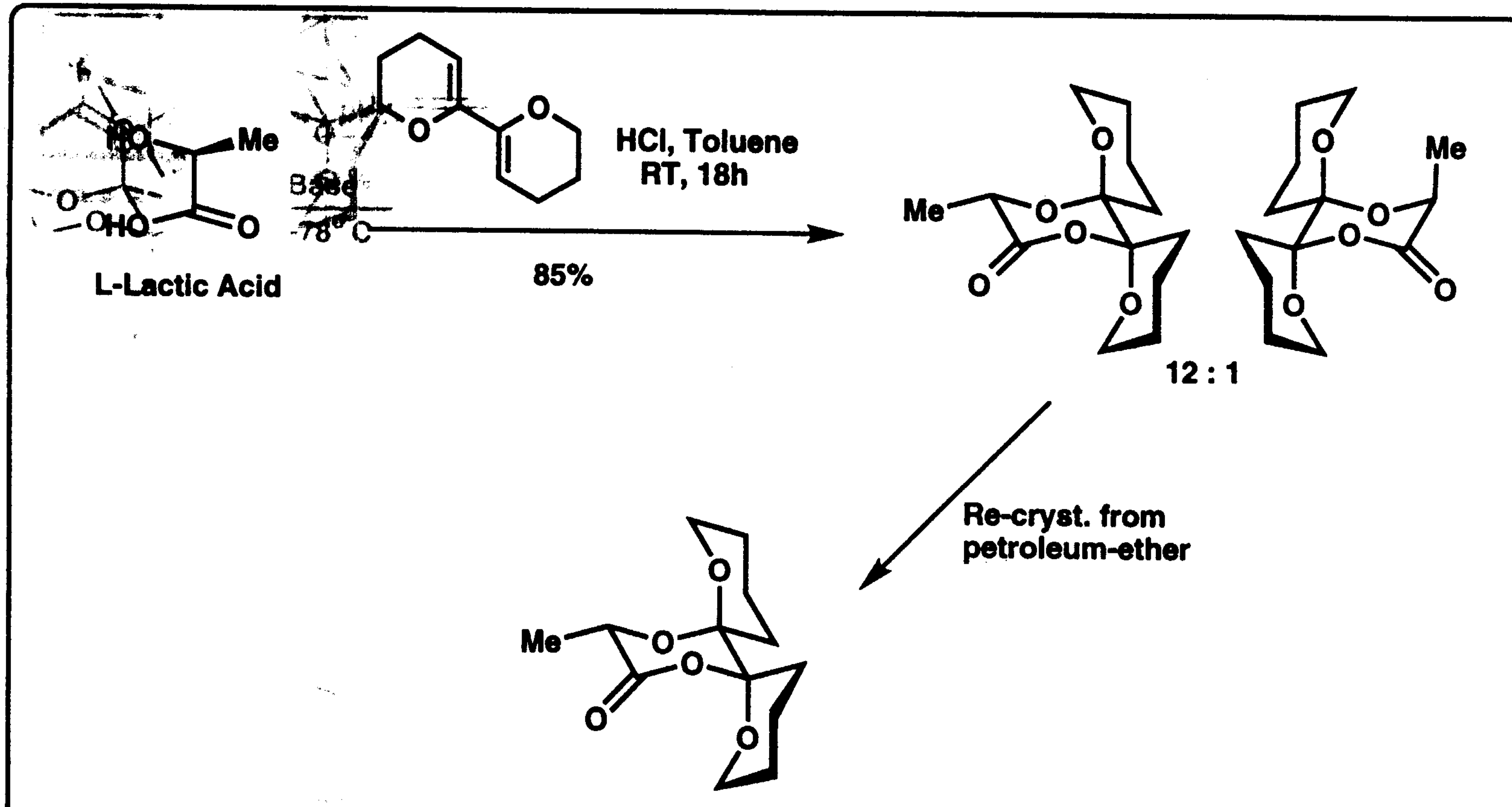
Preparation of 1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecane



Protection of Vicinal Diols : Selectivity over Protection of 1,3-Diols



Lactic Acid Dispiroketal Adducts



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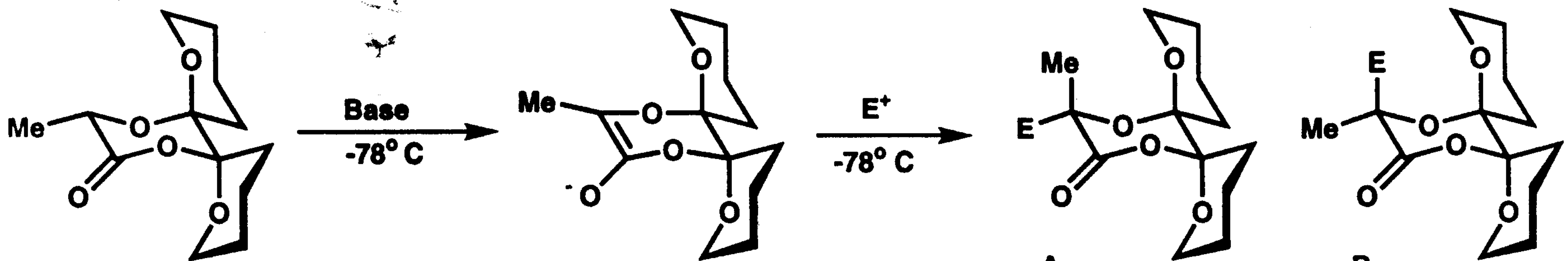
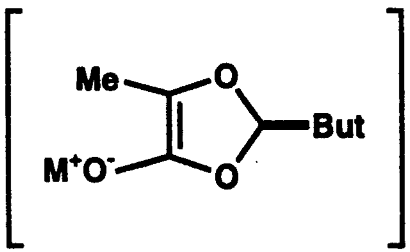
Down am, K.S.Ki ey,and

Lactic Dispiroketal Enolates



A B

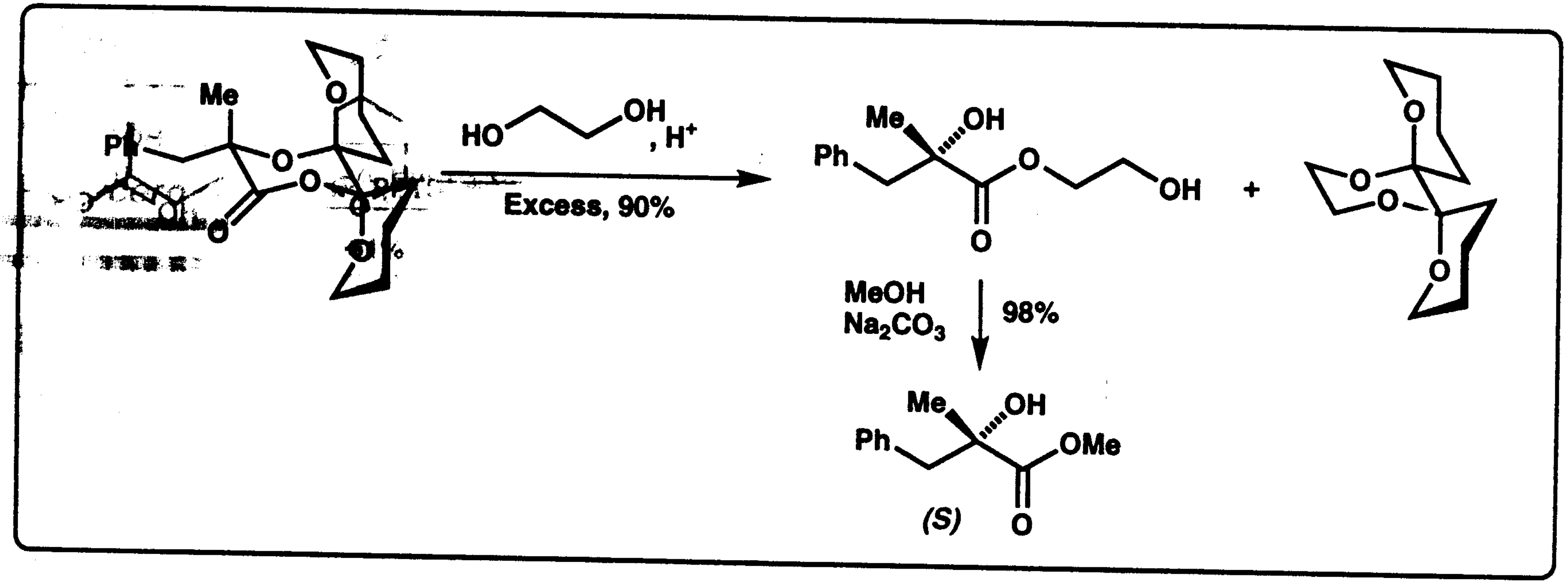


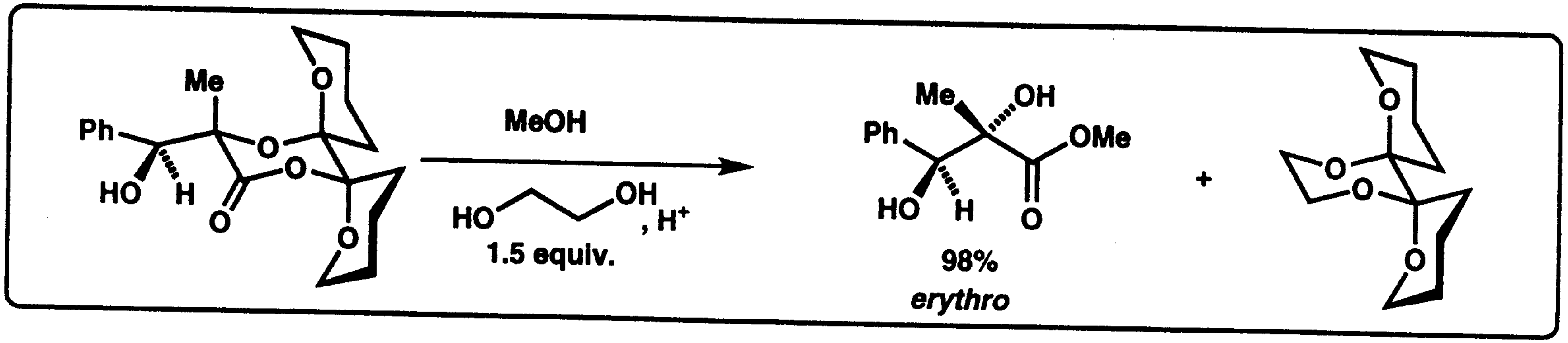
cf. Seebach Auxiliary

Electrophile	Ratio A : B	Yield
$PhCH_2Br$	99 : 1	86 %
AllylBr	96 : 4	94 %
EtI	89 : 11	75 %
nPrI	92 : 8	67 %
PhCHO	99 : 1 and > 96% d.e.	96 %
CH_2=CHCHO	99 : 1 and > 96% d.e.	94 %

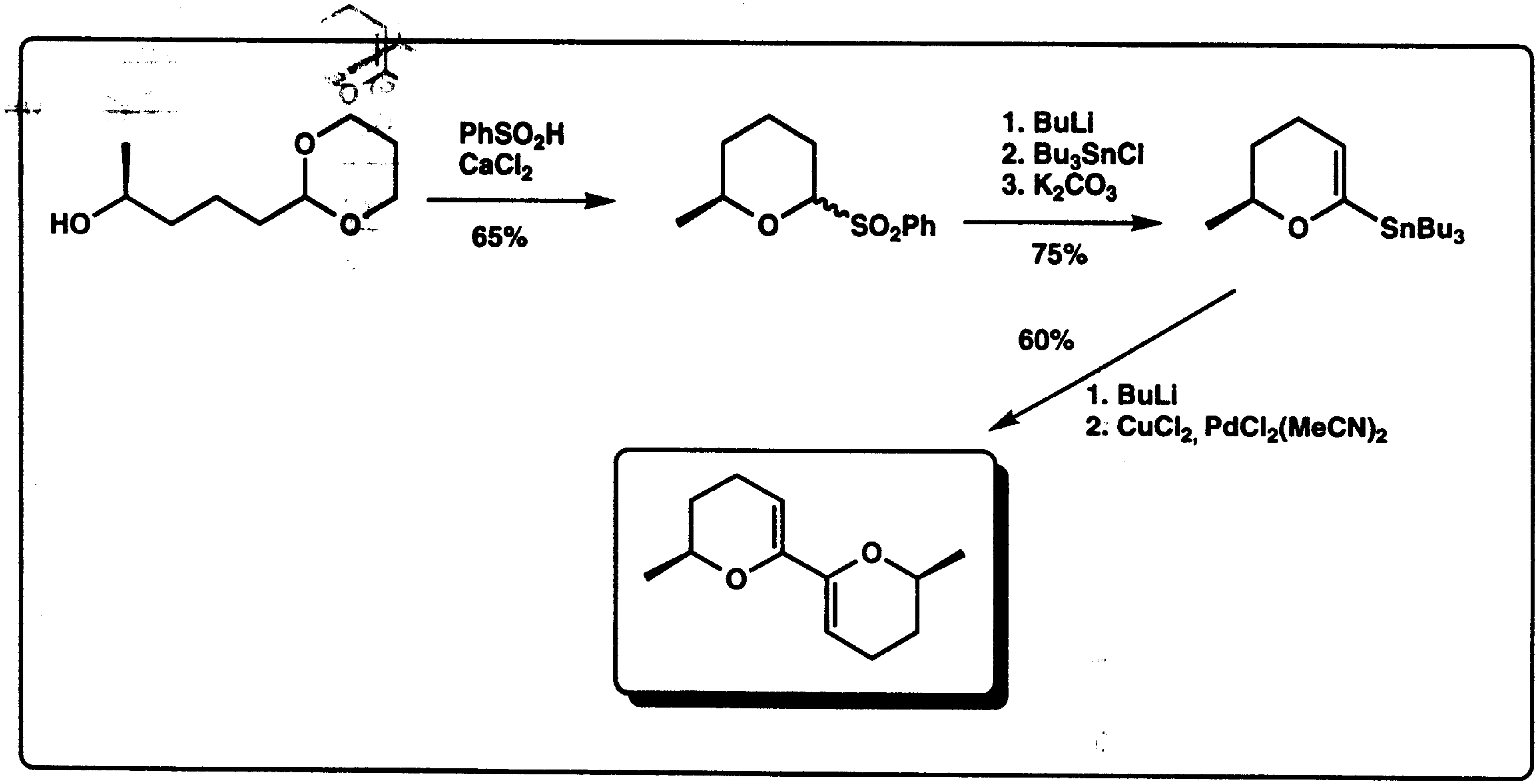
R.Downham, K.S.Kim, S.V.Ley,and M.Woods, *Tetrahedron Lett.*, 1994,*35*,769

Deprotection of Alkylated Adducts

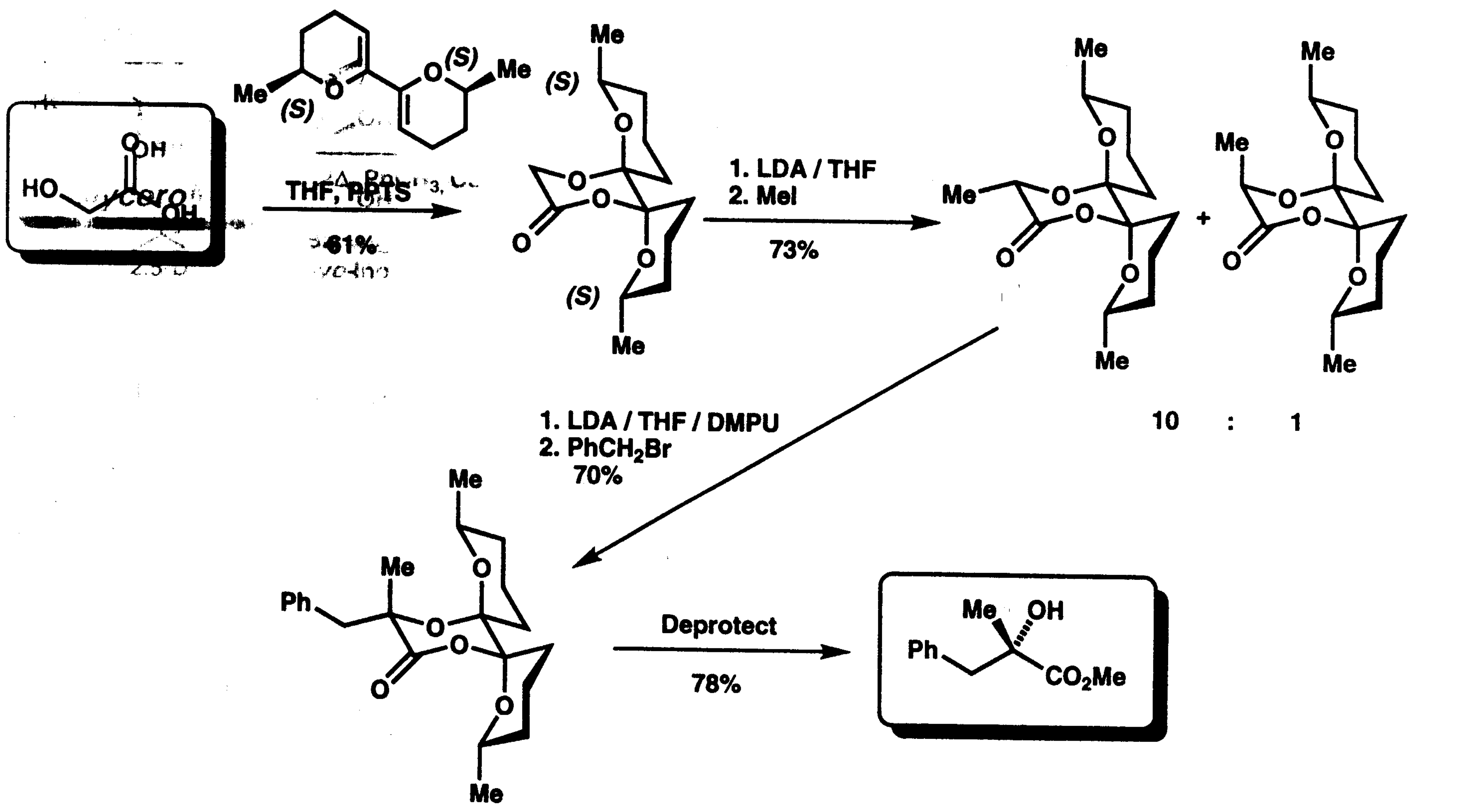




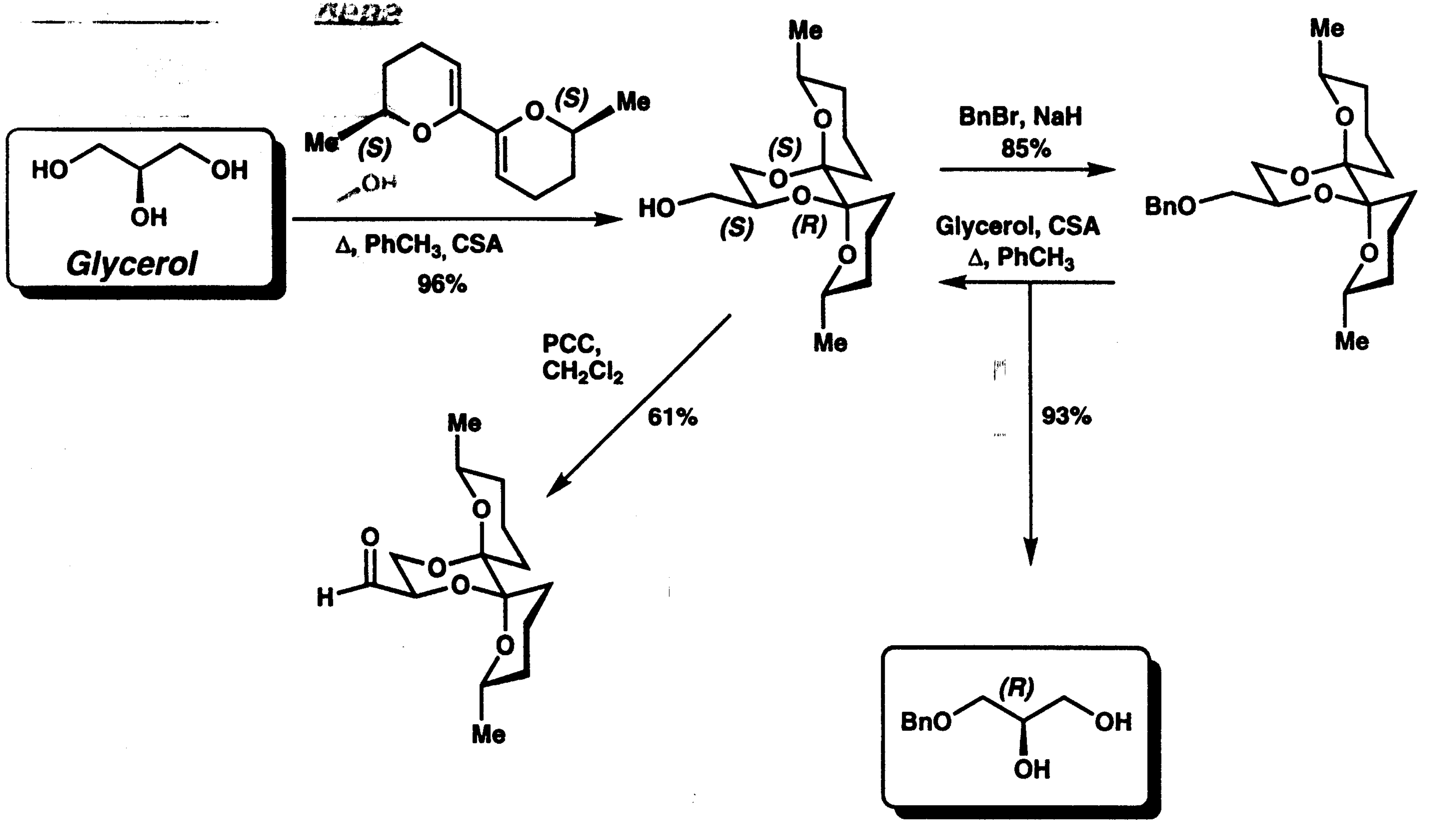
Synthesis of S,S-Dimethyl-bis-DHP



Glycolic Acid Dispiroketal Adducts

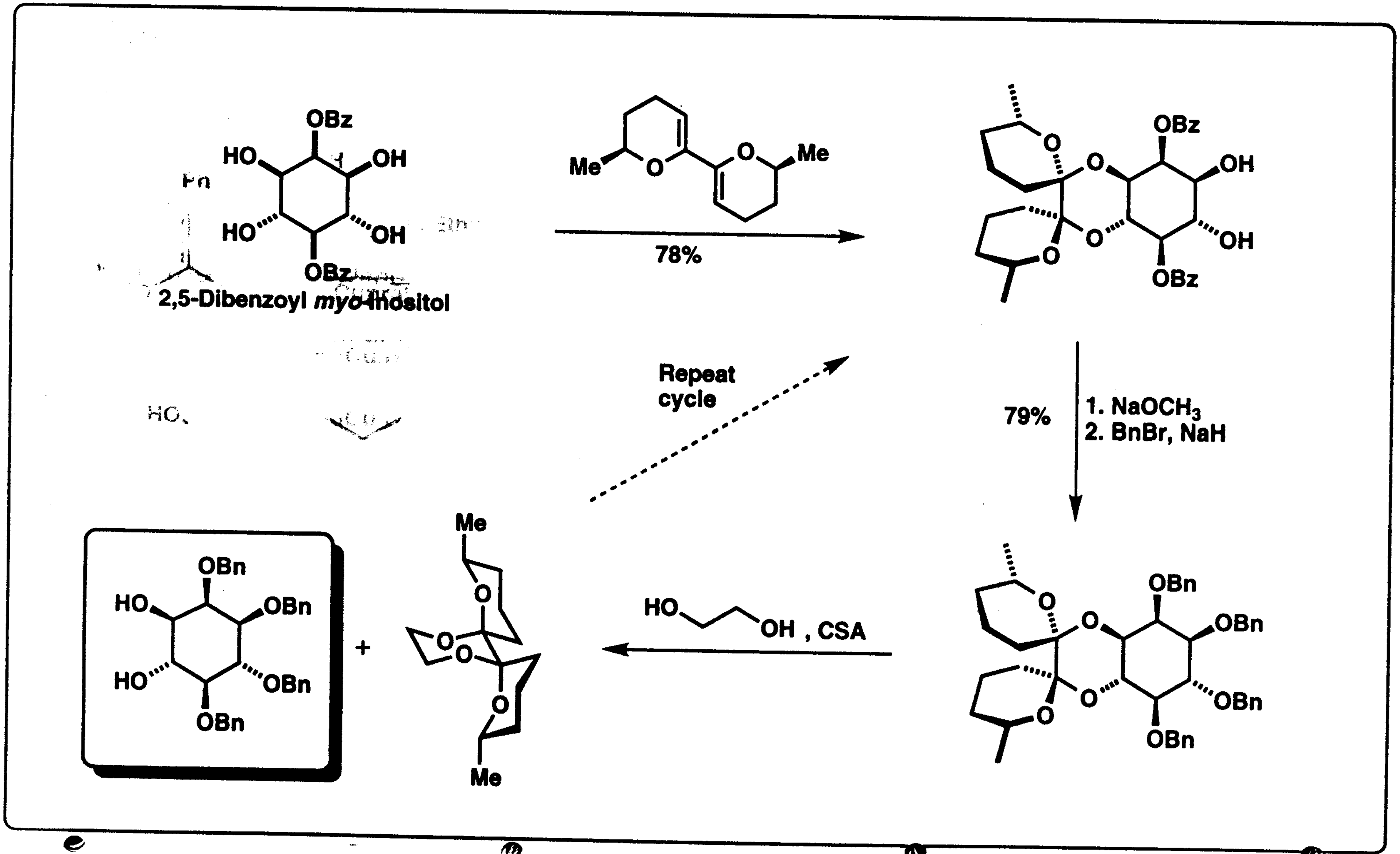


Desymmetrisation of Glycerol Using Chiral bis-DHP

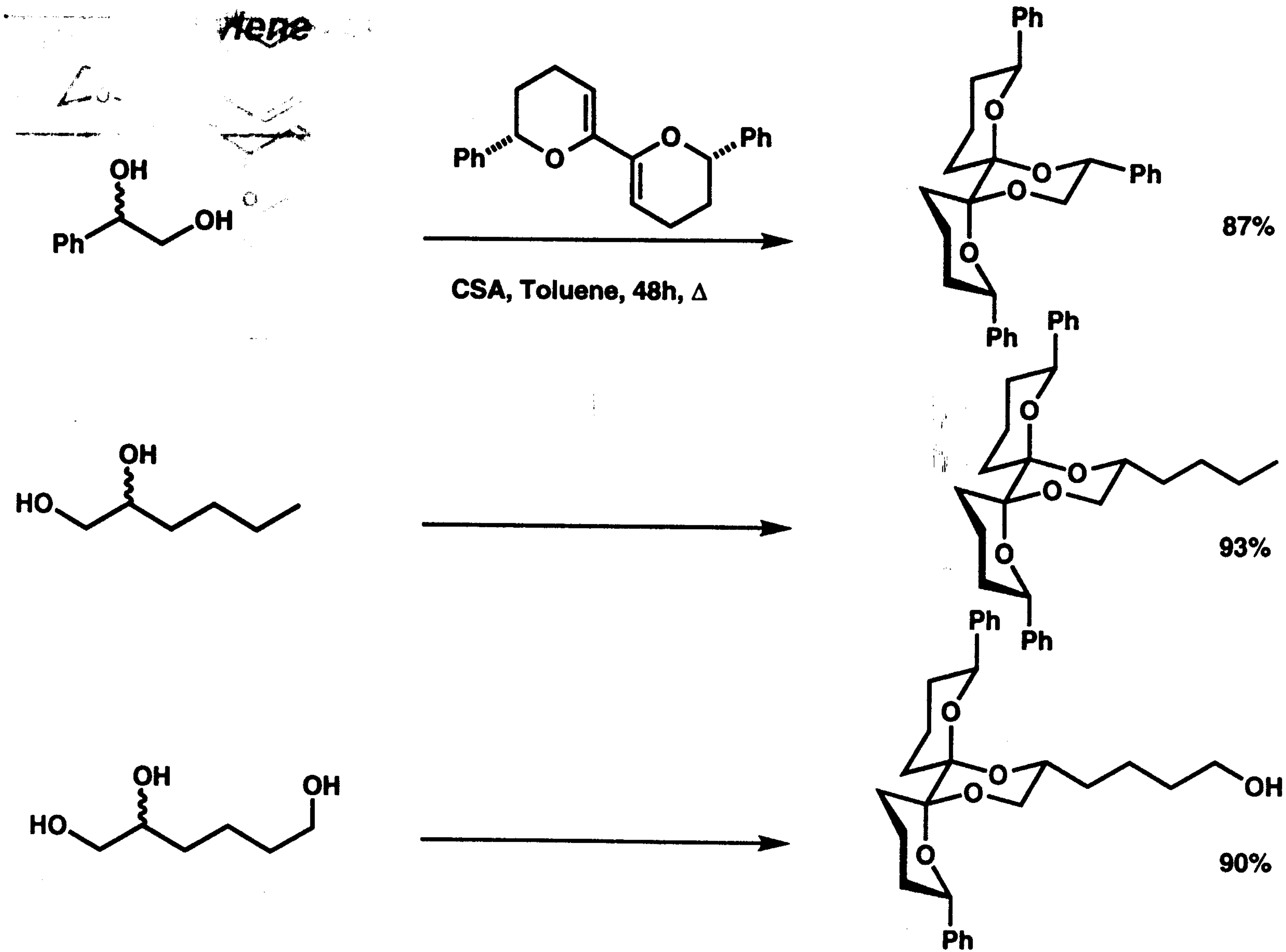


G-J.Boons, D.A.Entwistle, S.V.Ley and M.Woods, *Tetrahedron Lett.*, 1993, *34*, 5649.

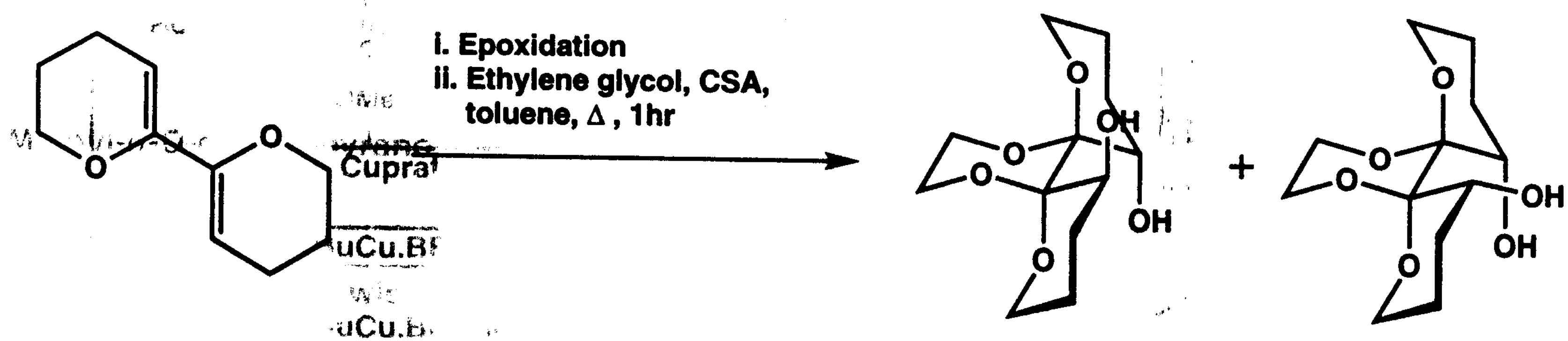
Desymmetrisation of myo-Inositol via Dimethyl-Dispiroketal Formation



Resolution of Vicinal Diols

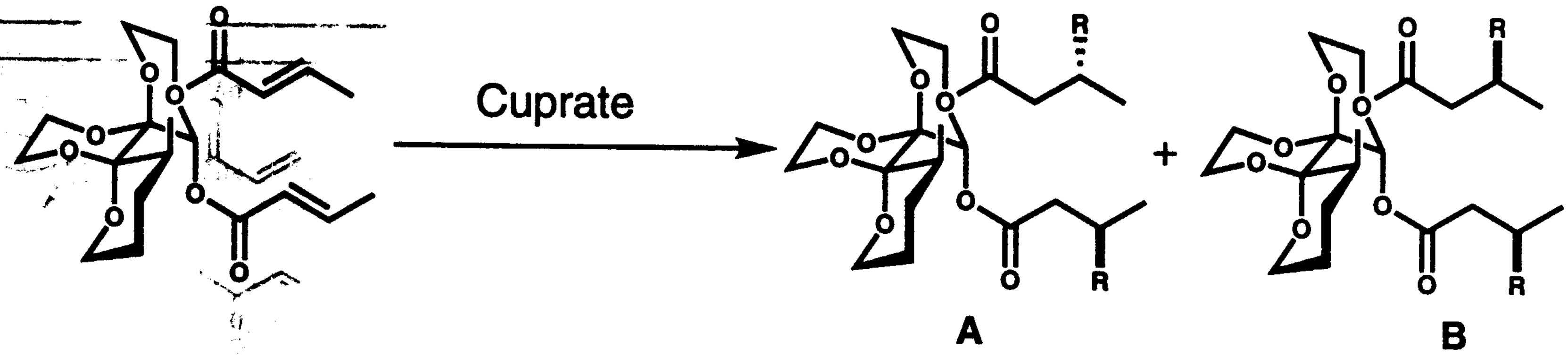


Double Epoxidation of bis-DHP and Reaction with Ethylene Glycol under Thermodynamic Conditions



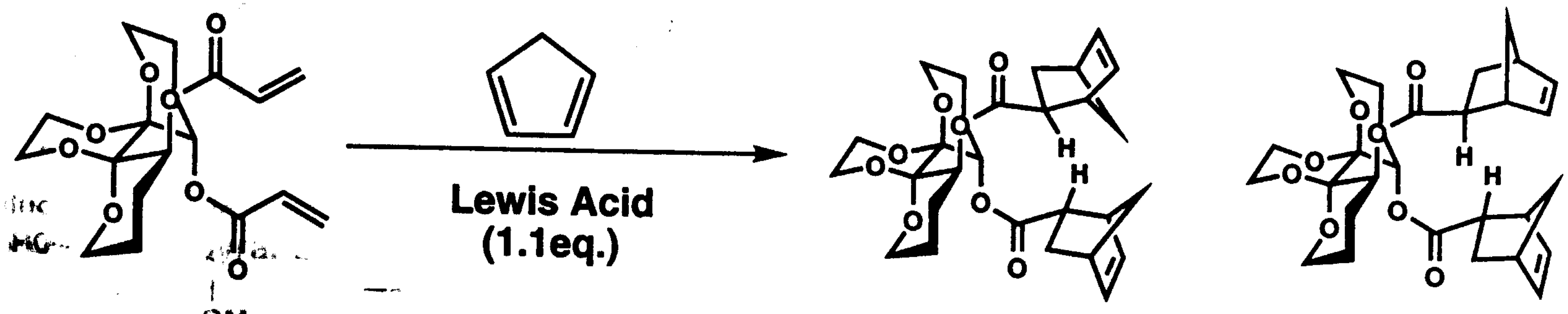
Epoxidation Conditions	Yield	Ratio
*m*CPBA, $NaHCO_3$, DCM, H_2O, 0˚C	62%	5:1
Dimethyl dioxirane, acetone, -78˚C	81%	1:2

Preliminary Results for Asymmetric Michael Additions into a Bifunctional Michael Acceptor



Cuprate	R	Temp, Time	Yield	Ratio A:B	Stereofacial Selectivity
$BuCu.BF_3.Bu_3P$	Bu	-45˚C, 16hrs	63%	89:11	89%
$BuCu.BF_3.Bu_3P$	Bu	-60˚C, 36hrs	57%	98:2	98%
$Bu_2CuCNLi_2$, $ZnCl_2$	Bu	-60˚C, 36hrs	80%	99:1	99%
BuMgCl, CuBr.DMS $ZnCl_2$	Bu	-60˚C, 12hrs	40%	71:29	71%
$Bu_2CuCNLi_2$	Bu	-60˚C, 12hrs	82%	–	35% opposite stereoselectivity

Asymmetric Cycloadditions of Cyclopentadiene to a Bifunctional Dienophile

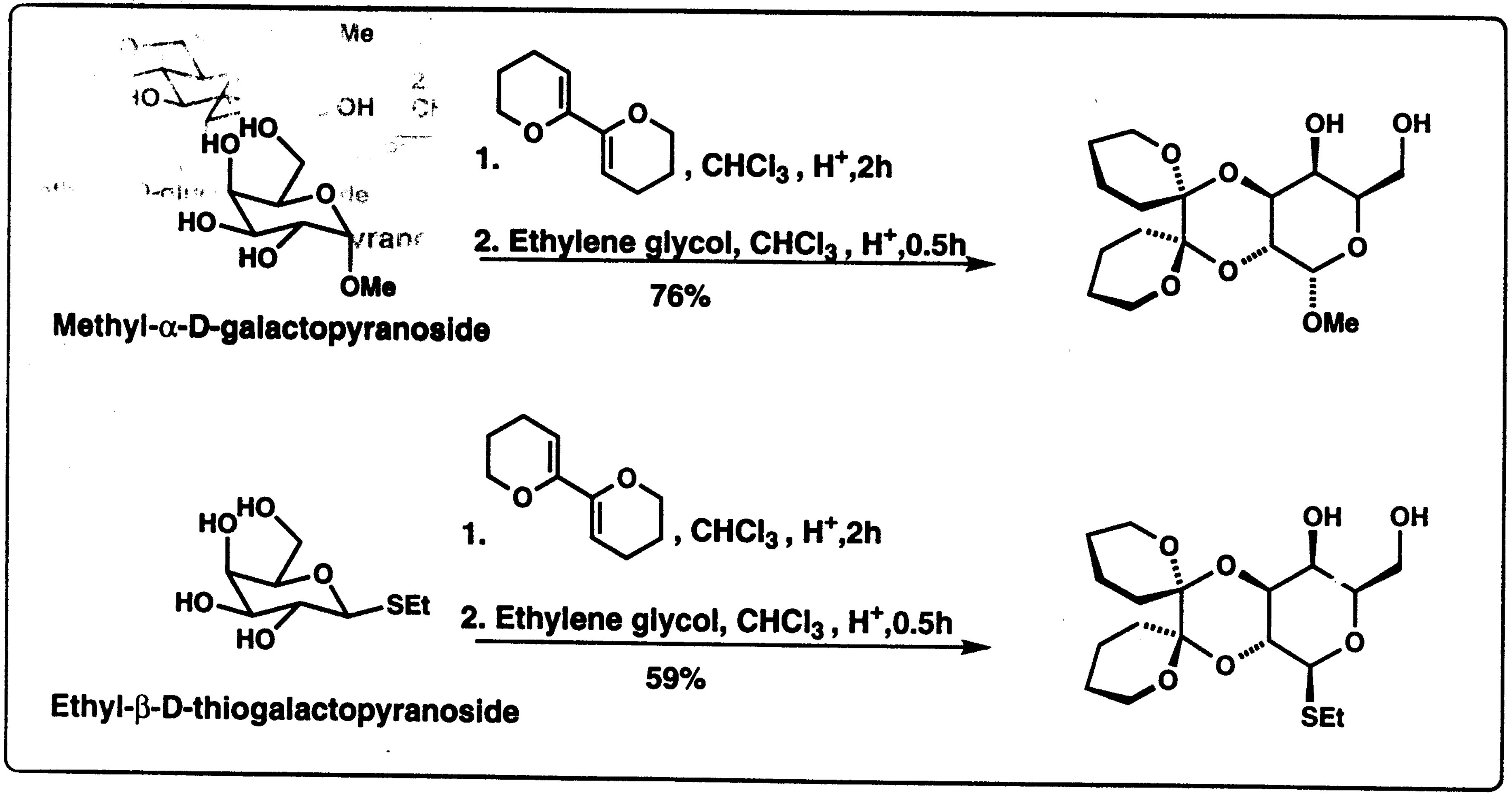


A

B

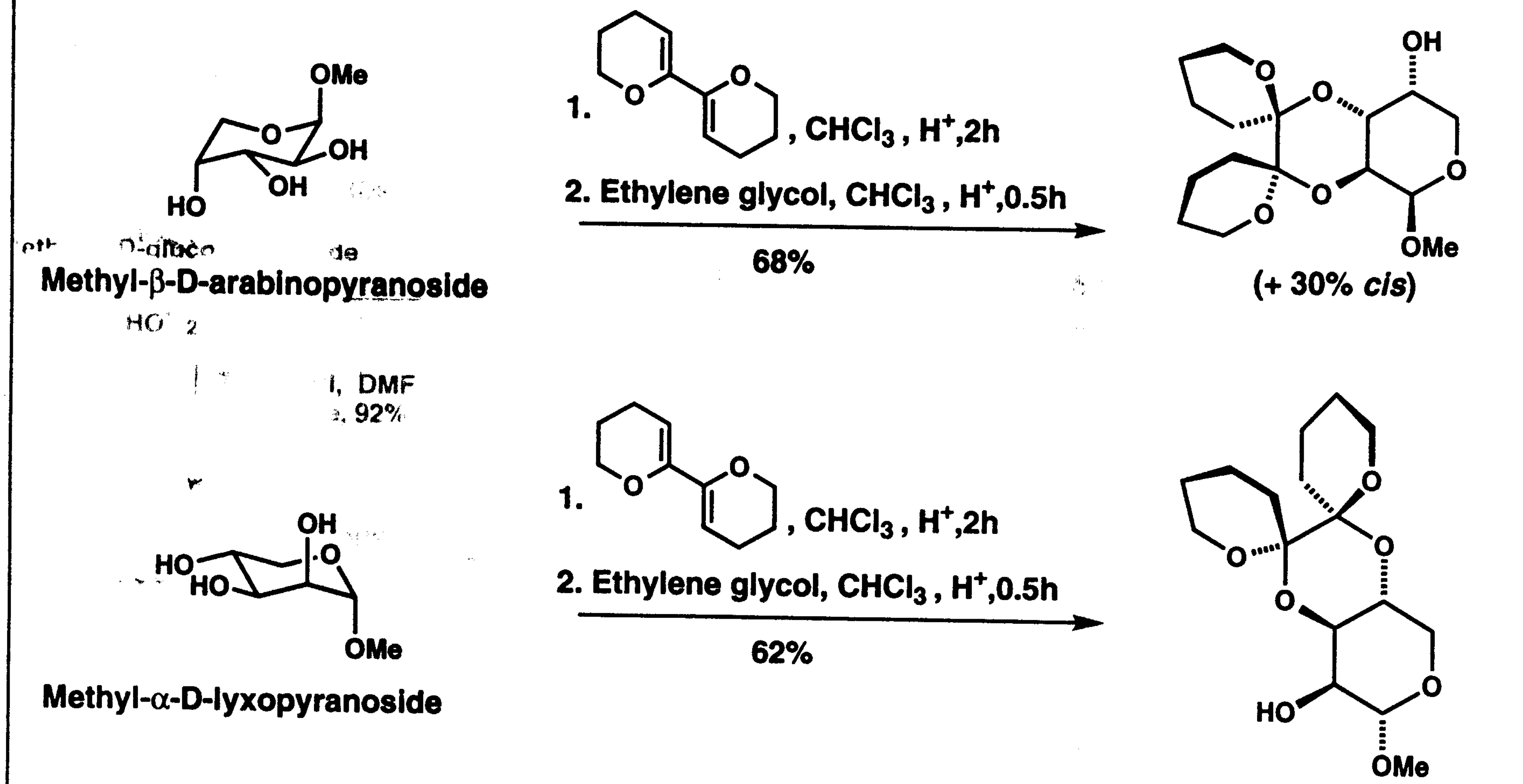
Lewis Acid	Solvent	Temp	Time	Yield A	Yield B	Ratio A:B	d.e. A wrt B
Et_2AlCl	DCM	-78°C	3hr	93	6	15.5:1	87%
Et_2AlCl	DCM	0°C	1hr	83	7	11.9:1	76%
Et_2AlCl	Toluene	0°C	1.5hr	85	9	9.4:1	76%
$SnCl_4$	Toluene	0°C	3.5hr	7	5	1.4:1	2%

One-Pot Selective Protection of Trans Diequatorial Vicinal Diols in Sugars



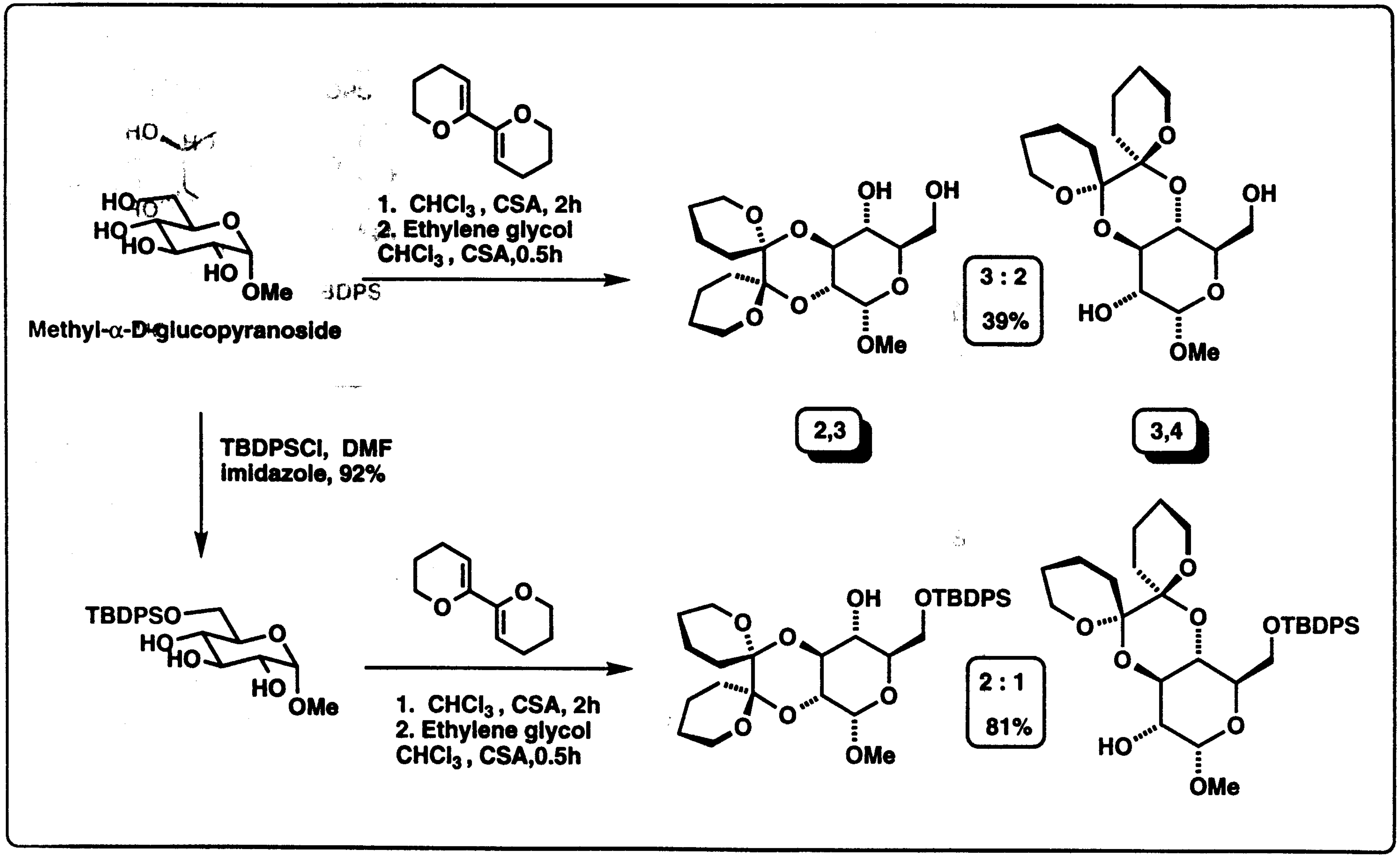
S.V.Ley, R.Leslie, P.D.Tiffin and M.Woods, *Tetrahedron Lett.*, 1992, *33*, 4767.

Arabinose and Lyxose



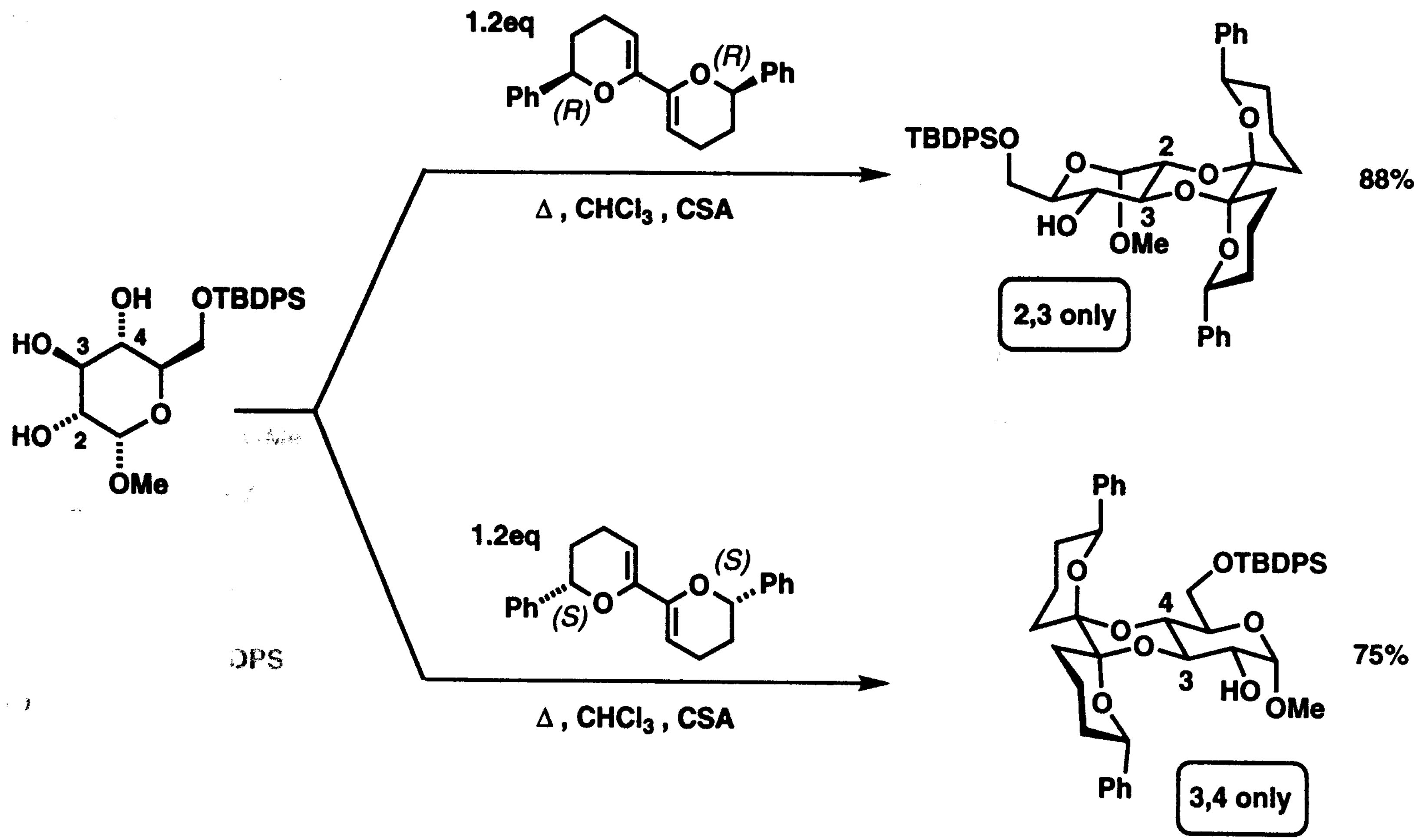
S.V.Ley, G-J.Boons, R.Leslie, M.Woods and D.M.Hollinshead, *Synthesis*,1993,689.

Dispiroketal Protection of Glucopyranosides



A.B.Hughes, S.V.Ley, H.W.M.Priepke and M.Woods, *Tetrahedron Lett.*, 1994, *35*, 773.

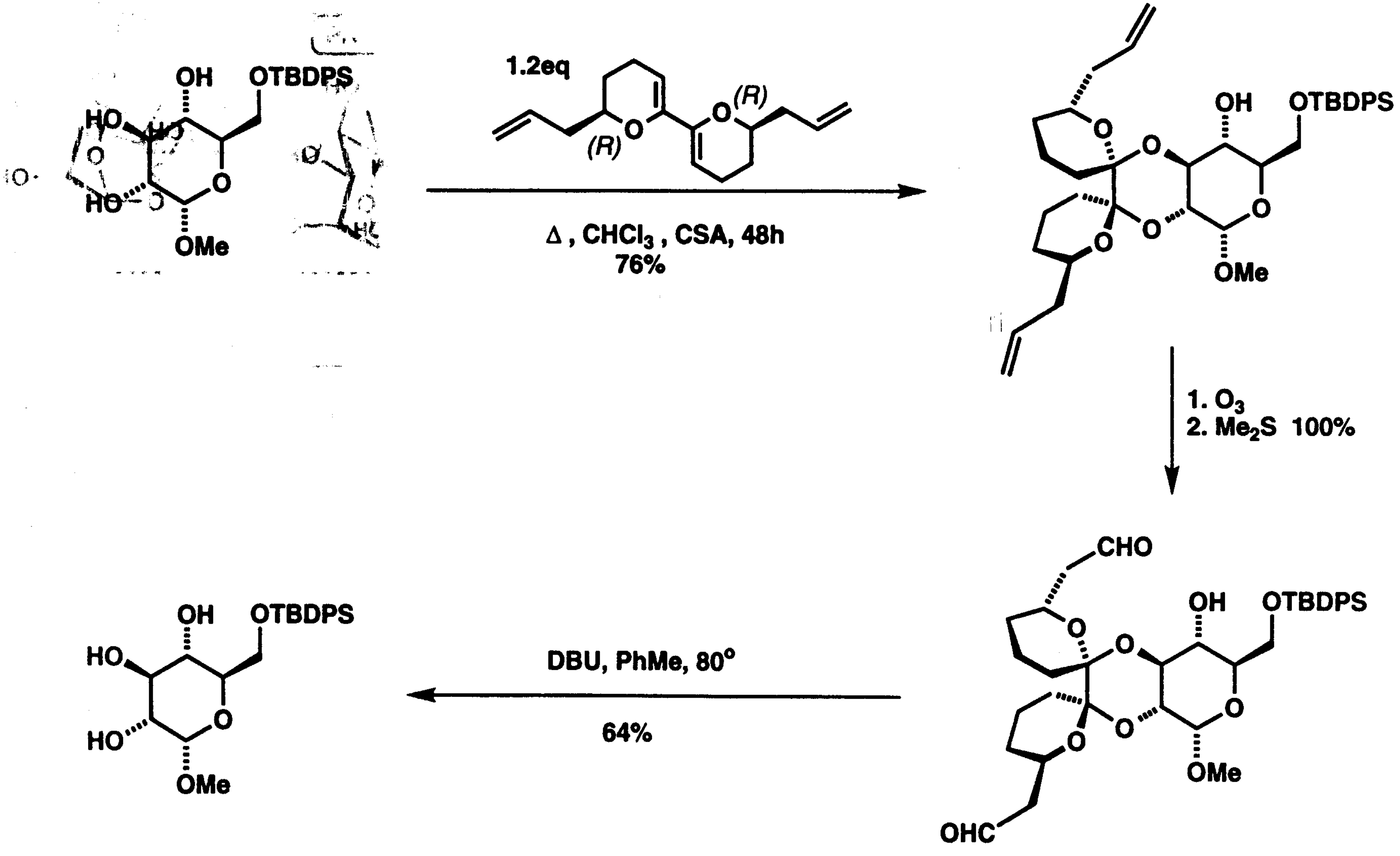
Enantiomeric Vicinal Diol Recognition



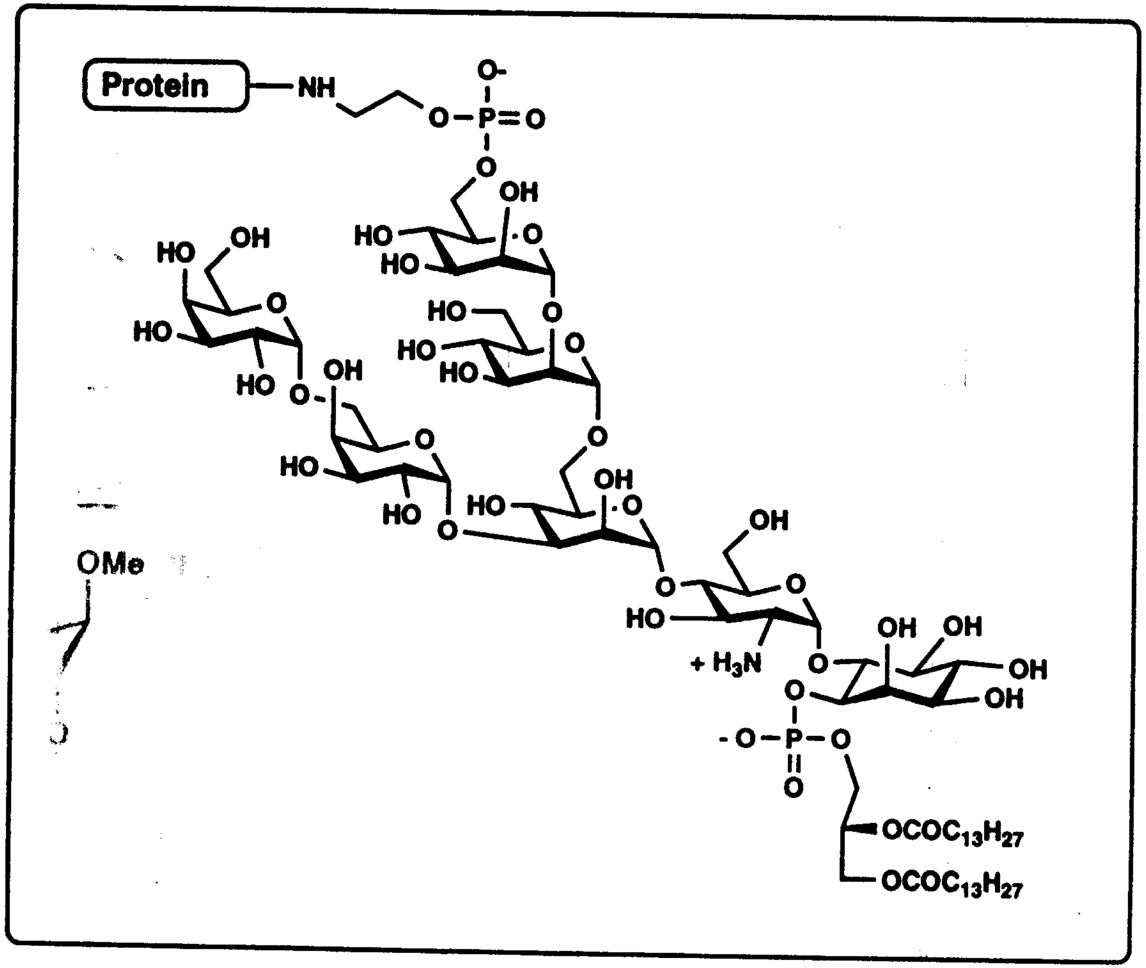
Deprotected by : $FeCl_3$, CH_2Cl_2 , 10h at RT

D.A.Entwistle, A.B.Hughes, S.V.Ley and G.Visentin, *Tetrahedron Lett.*, 1994, 35, 777.

R,R- Bisallyl-Dispoke Protection



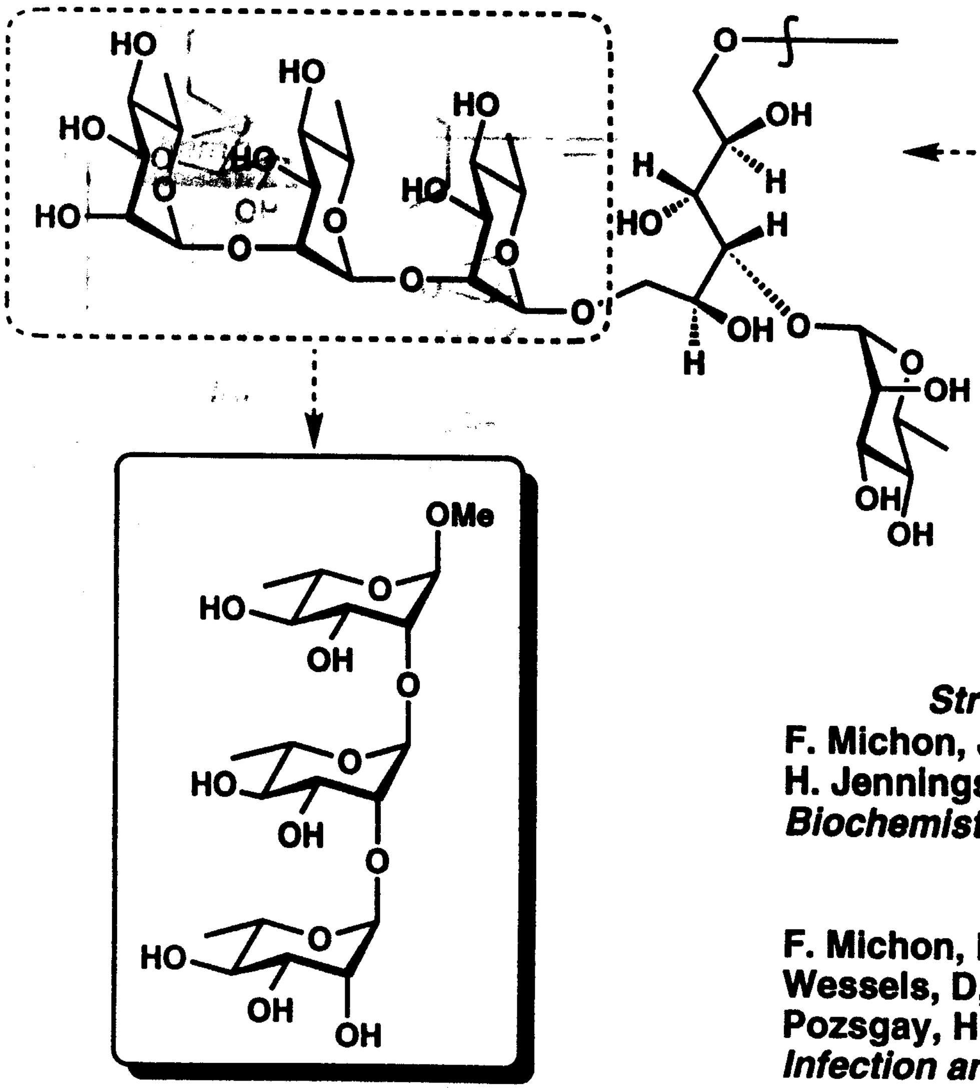
Variant Surface Glycoprotein of Trypanosoma brucei



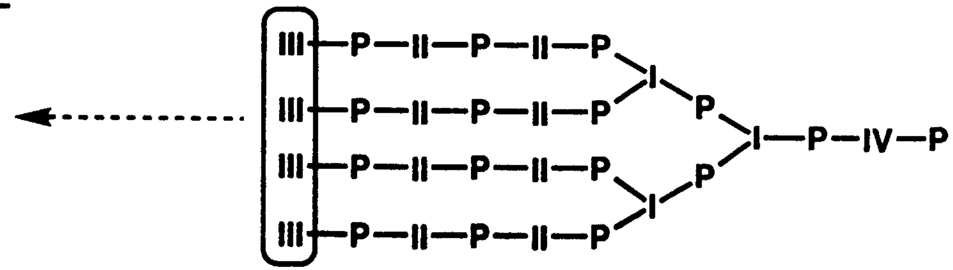
Ferguson, M.A.J., Homans, S.W., Rademacher, T.W. *Science* 1988, *239*, 753

Common Polysaccharide Antigen of Group B Streptococci

Fragment III



Proposed Structure for Antigen



I 11 sugar residues
II 8 sugar residues
III 5 sugar residues
IV 9 sugar residues

Total 126 sugar residues!

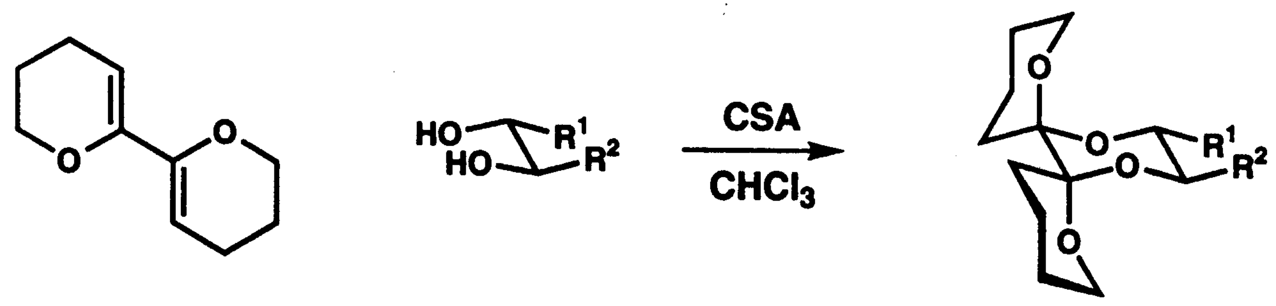
Structure Determination

F. Michon, J. Brisson, A. Dell, D. Kasper, H. Jennings
Biochemistry 27 5341 (1988)

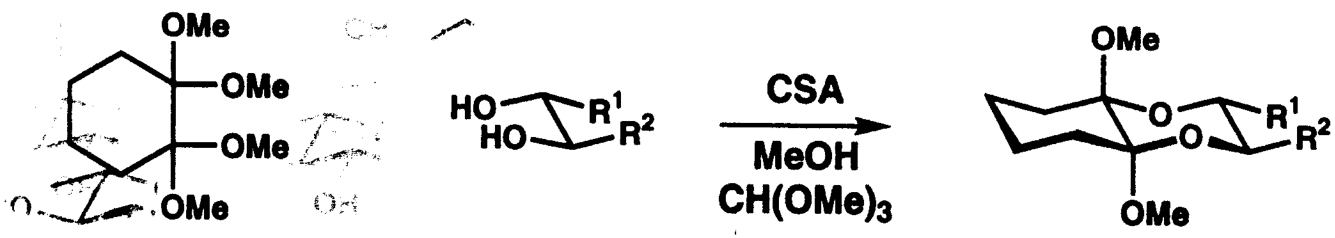
Immunology

F. Michon, R. Chalifour, R. Feldman, M. Wessels, D, Kasper, A. Gamian, V. Pozsgay, H. Jennings
Infection and Immunity 59(5) 1690 (1991)

Dispoke and new *Cyclohexyl DIAcetal CDA Protection Method*

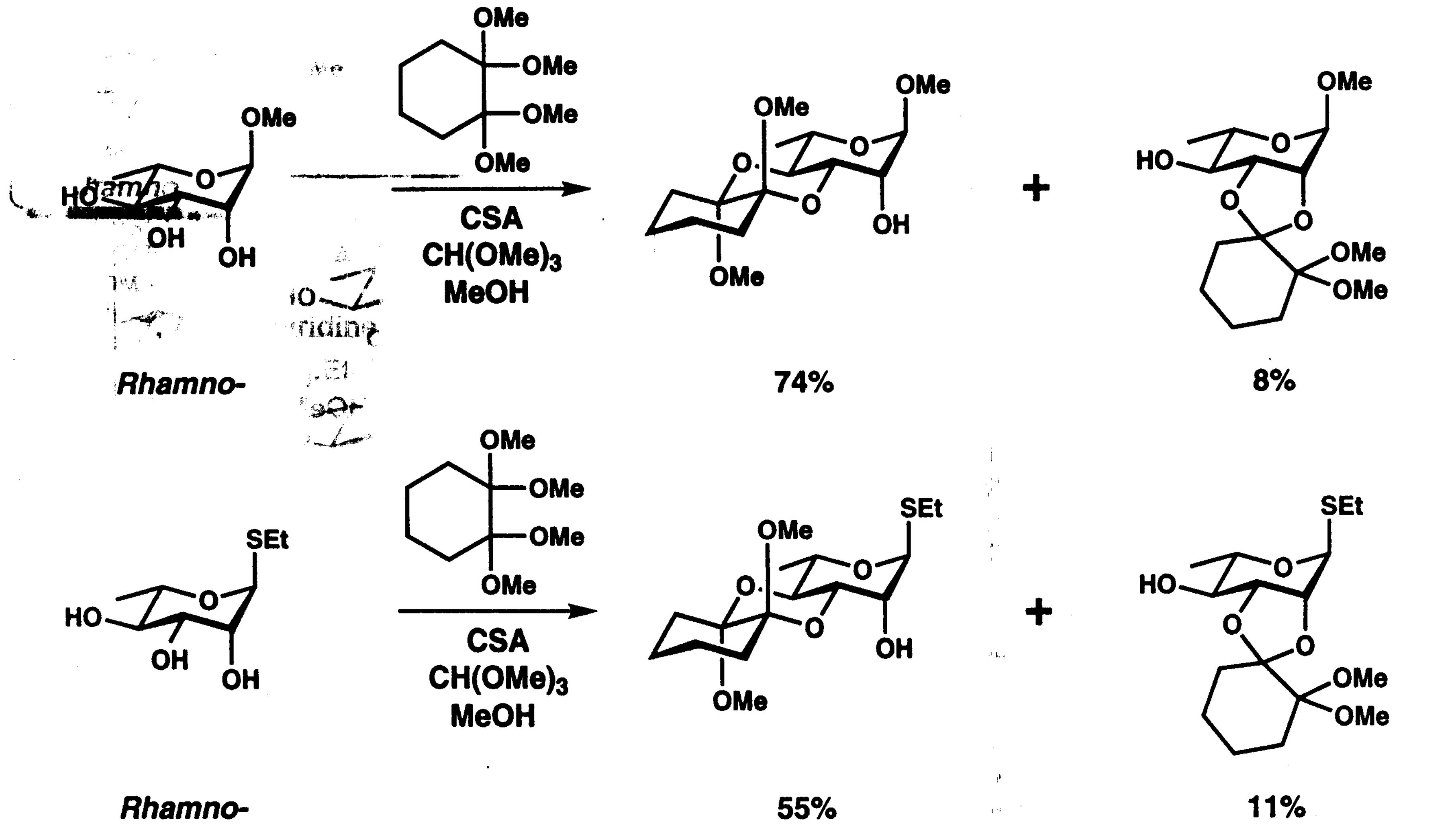


Four anomeric effects
Four equatorial alkyl sidechains

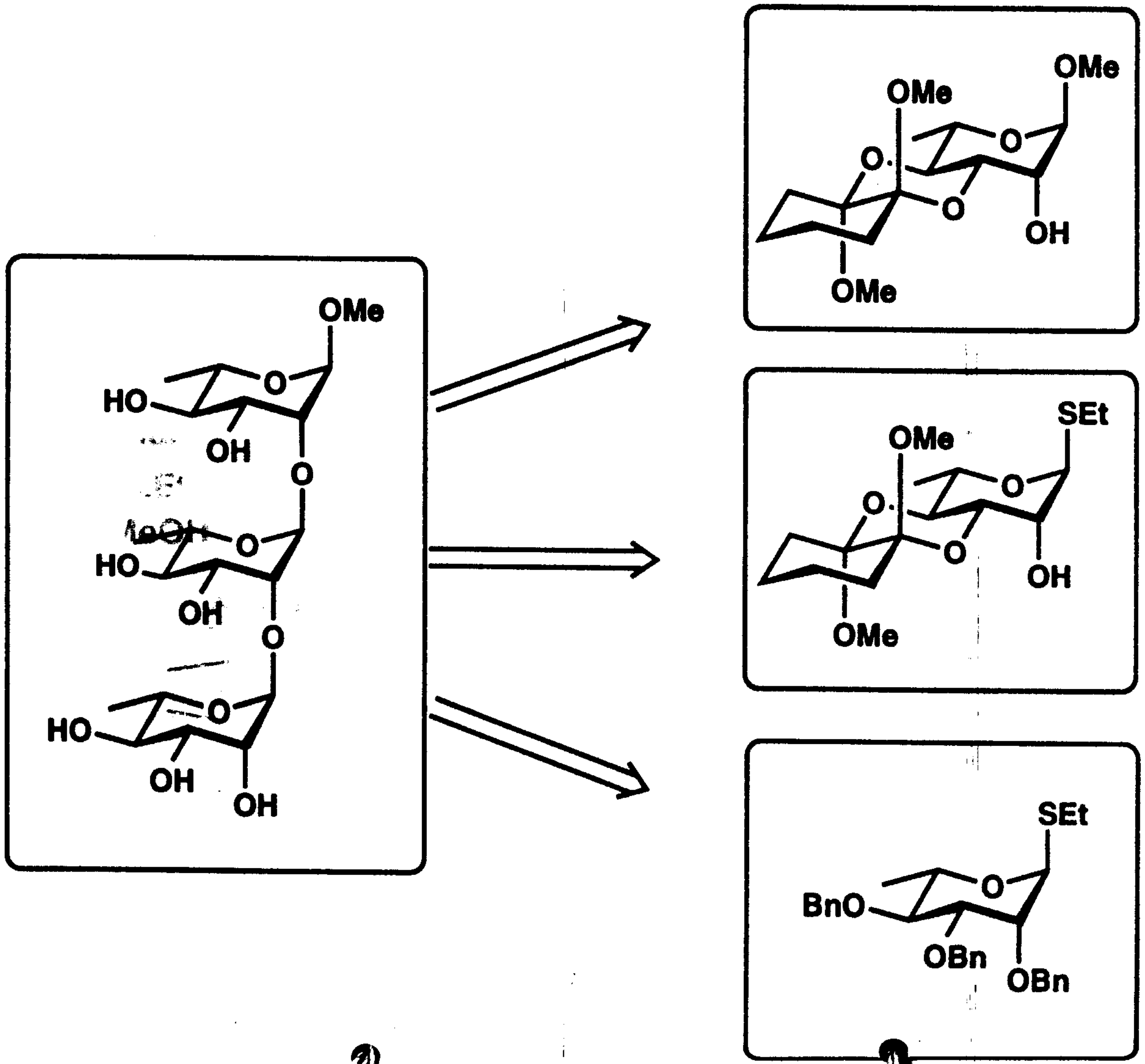


Four anomeric effects
Four equatorial alkyl sidechains

CDA Protection:
Rhamno-*pyranosides*



Rhamnose Trisaccharide: Retrosynthetic Analysis

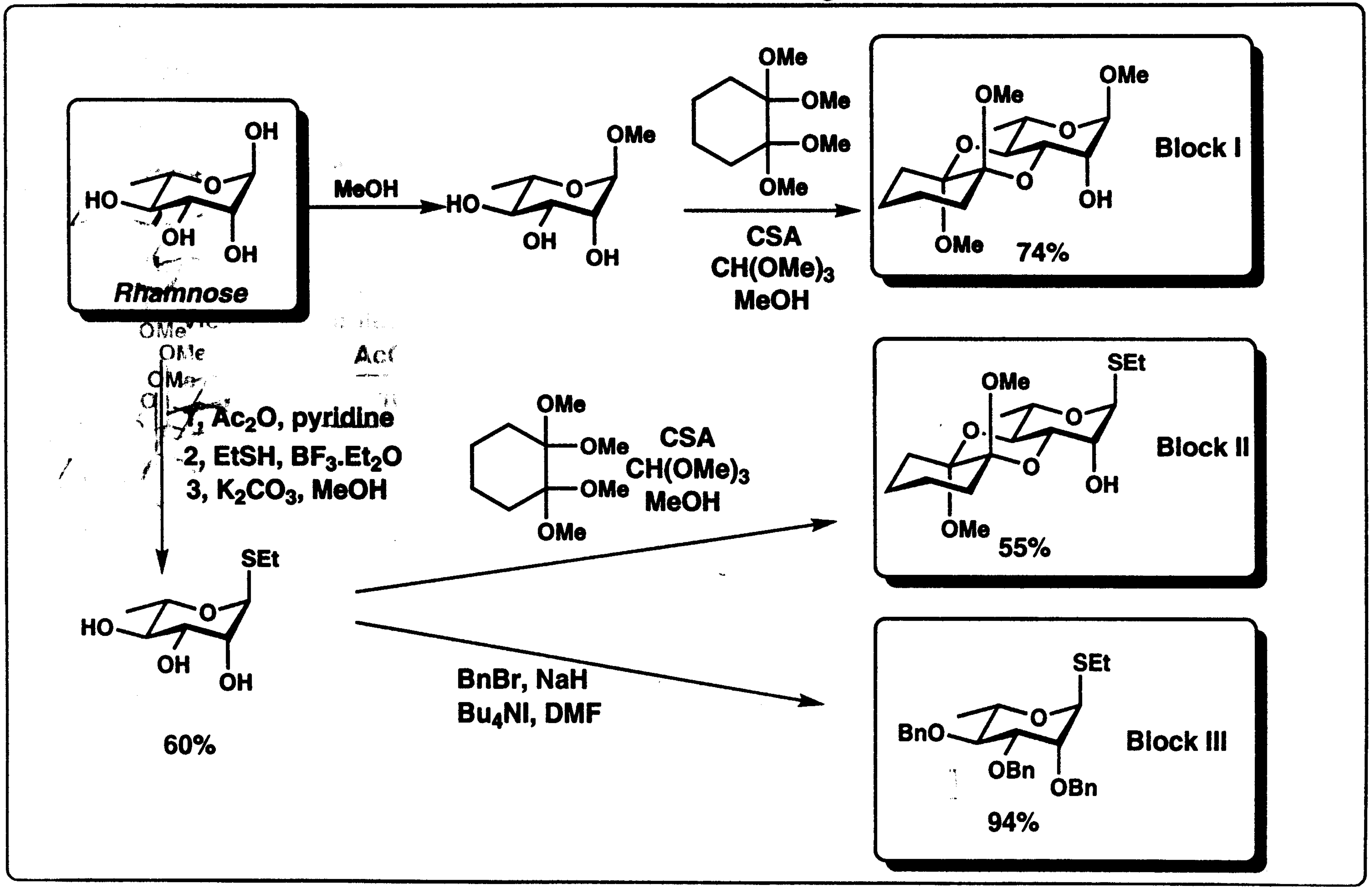


Building Block I

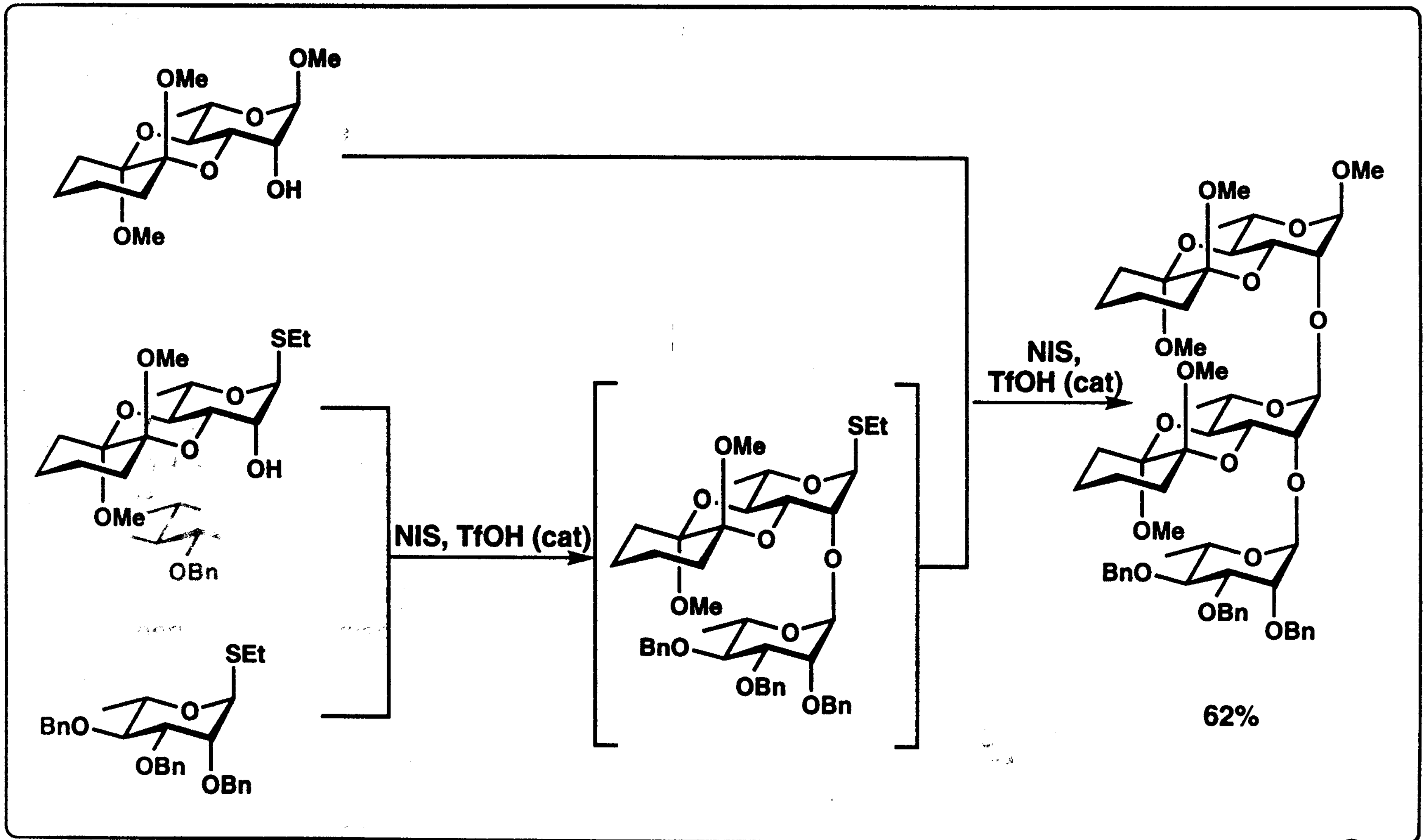
Building Block II

Building Block III

Rhamnose Trisaccharide: Monosaccharide Building Blocks



Rhamnose Trisaccharide: One Pot Synthesis



Rhamnose Trisaccharide: Deprotection