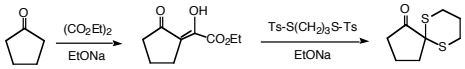
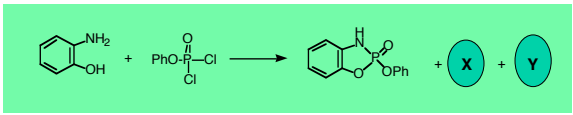
第７９回応用化学科セミナー
２００４年７月５日

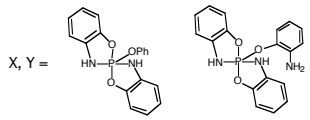
予想通りの実験結果が出ても面白くない

愛媛大学工学部応用化学科　渡辺　裕

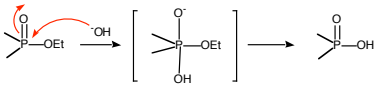


反応をよく知る
様子をよく観察する

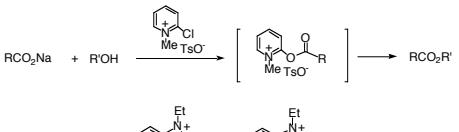


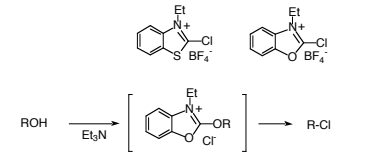


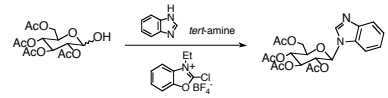
五配位中間体の存在を示唆

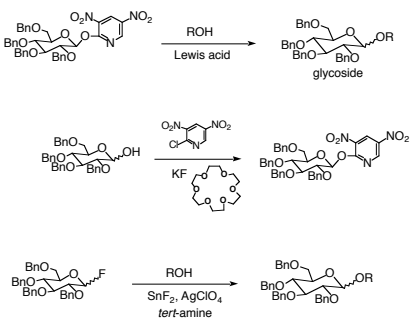


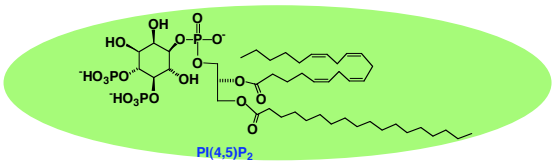
五配位中間体





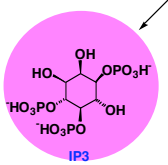




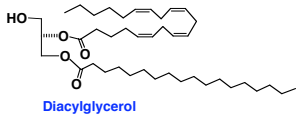


PI(4,5)P2
Phosphatidylinositol 4,5-bisphosphate
from beef brain

イノシトール

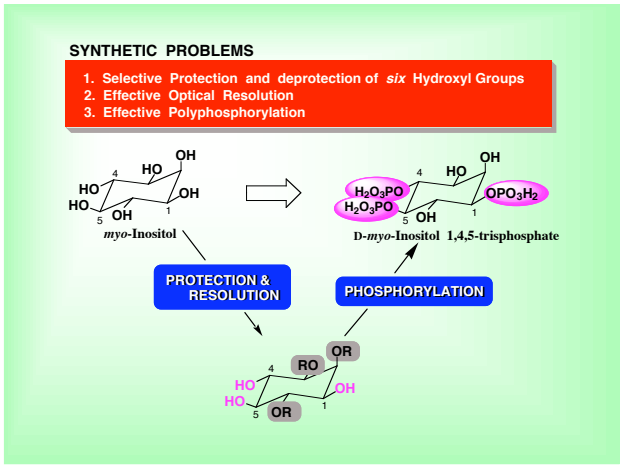


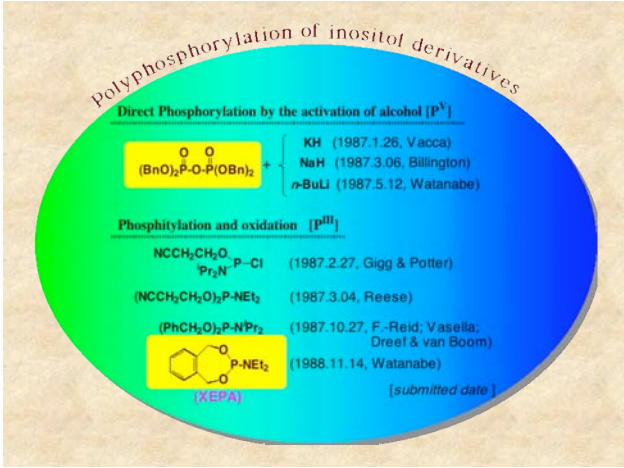
IP3
(Ins1,4,5-P3)

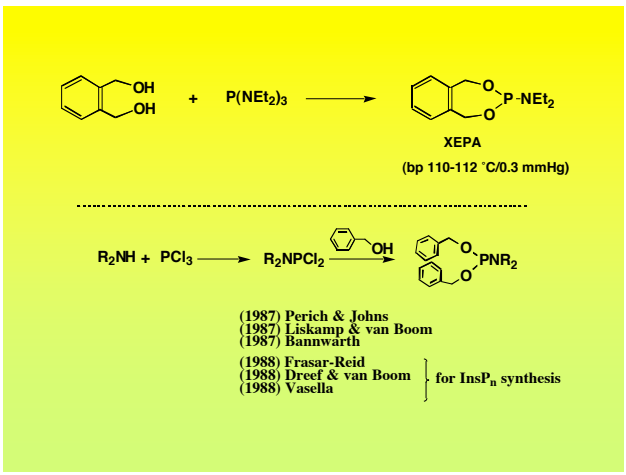


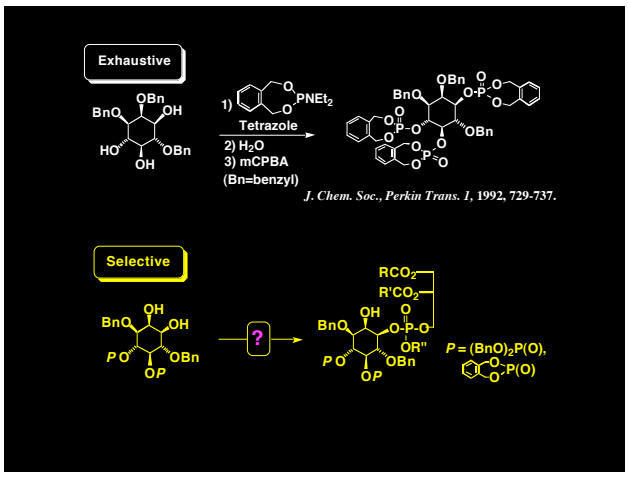
Diacylglycerol

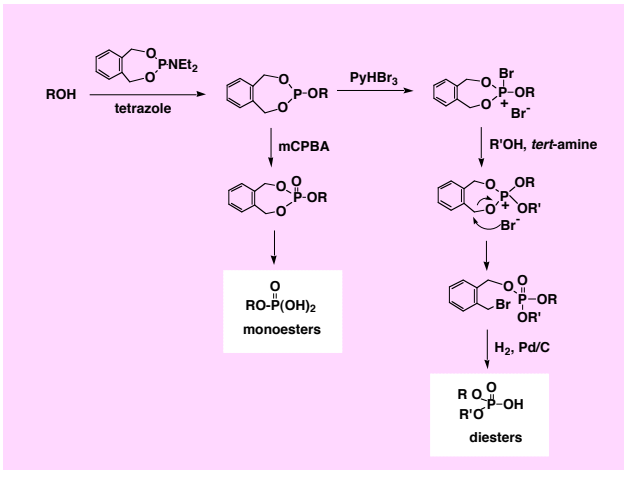
(C. E. Ballou, 1961)

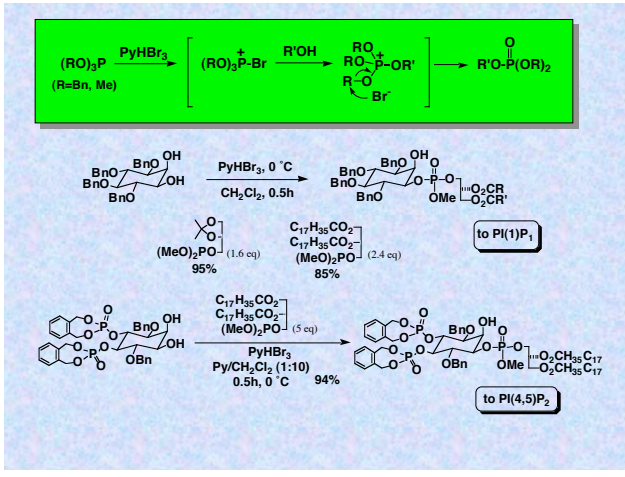

SYNTHETIC PROBLEMS
1. Selective Protection and deprotection of six Hydroxyl Groups
2. Effective Optical Resolution
3. Effective Polyphosphorylation
myo-Inositol
D-myo-Inositol 1,4,5-trisphosphate
PROTECTION & RESOLUTION
PHOSPHORYLATION

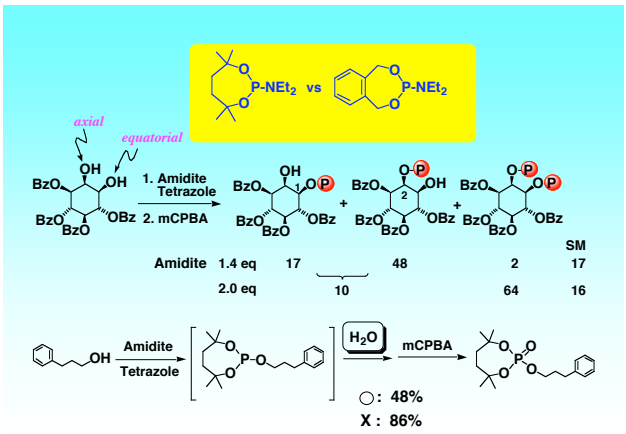

Polyphosphorylation of inositol derivatives
Direct Phosphorylation by the activation of alcohol [P^V]
KH (1987.1.26, Vacca)
NaH (1987.3.06, Billington)
n-BuLi (1987.5.12, Watanabe)
Phosphitylation and oxidation [P^III]
(1987.2.27, Gigg & Potter)
(1987.3.04, Reese)
(1987.10.27, F.-Reid; Vasella; Dreef & van Boom)
(1988.11.14, Watanabe)
(XEPA)
[submitted date]

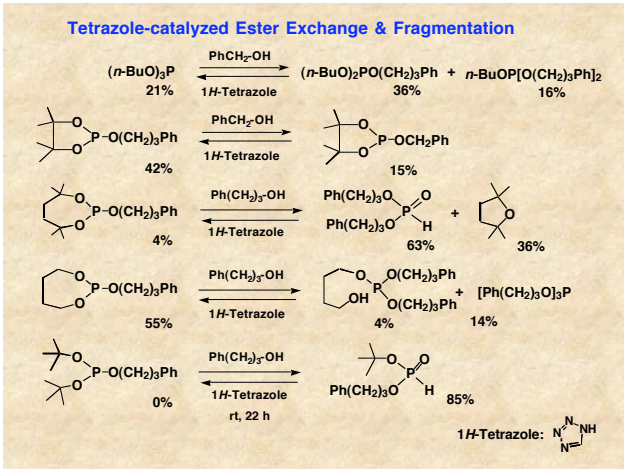

XEPA
(bp 110-112 °C/0.3 mmHg)
(1987) Perich & Johns
(1987) Liskamp & van Boom
(1987) Bannwarth
(1988) Frasar-Reid
(1988) Dreef & van Boom
(1988) Vasella
for InsP_n synthesis

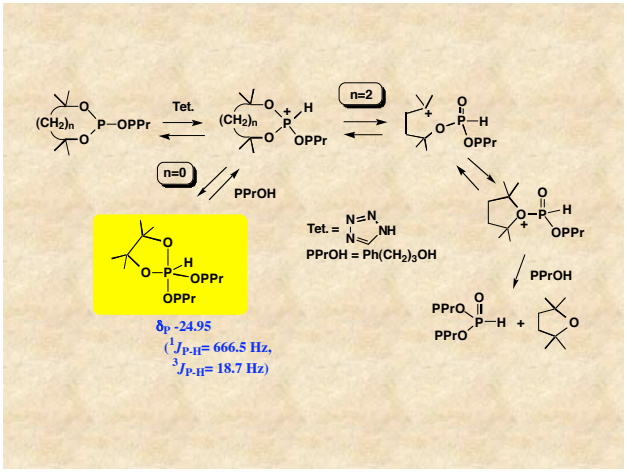

Exhaustive
Tetrazole
2) H2O
3) mCPBA
(Bn=benzyl)
J. Chem. Soc., Perkin Trans. 1, 1992, 729-737.
Selective
P = (BnO)2P(O),

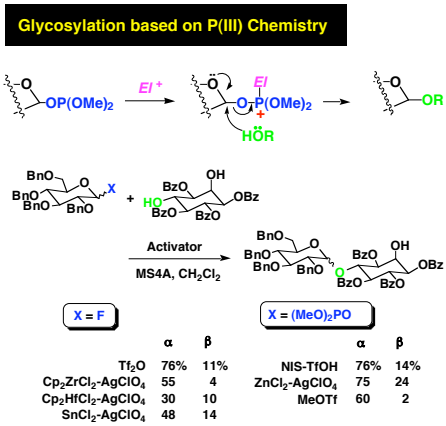

tetrazole
PyHBr3
mCPBA
R'OH, tert-amine
monoesters
H2, Pd/C
diesters

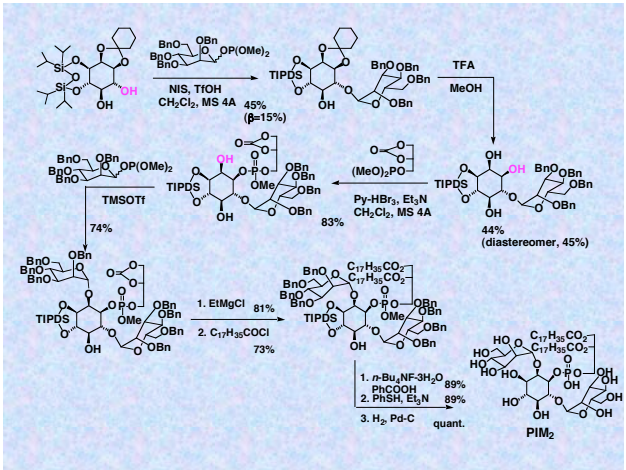

(R=Bn, Me)
PyHBr3, 0 °C
CH2Cl2, 0.5h
95%
85%
to PI(1)P1
Py/CH2Cl2 (1:10)
0.5h, 0 °C
94%
to PI(4,5)P2

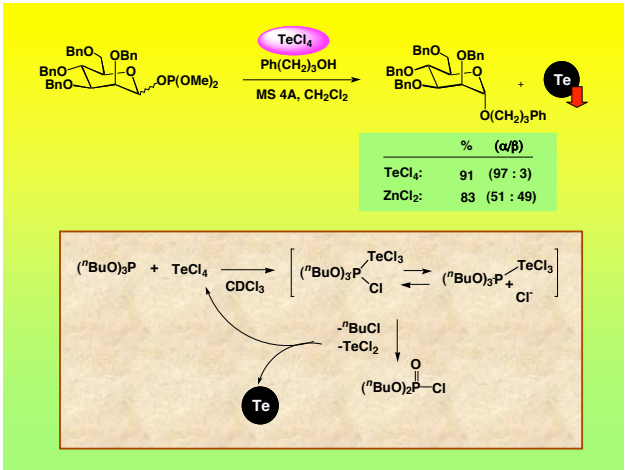

P-NEt2 vs P-NEt2
axial
equatorial
1. Amidite Tetrazole
2. mCPBA
Amidite 1.4 eq 17 48 2 17
2.0 eq 10 64 16
SM
Amidite Tetrazole
H2O
mCPBA
○: 48%
X : 86%


Tetrazole-catalyzed Ester Exchange & Fragmentation
PhCH2-OH
1H-Tetrazole
(n-BuO)3P 21%
(n-BuO)2PO(CH2)3Ph 36%
n-BuOP[O(CH2)3Ph]2 16%
42%
15%
4%
Ph(CH2)3-OH
63%
36%
55%
14%
0%
rt, 22 h
85%
1H-Tetrazole:


Tet.
n=2
n=0
PPrOH
Tet. =
PPrOH = Ph(CH2)3OH
δP -24.95
(1JP-H= 666.5 Hz,
3JP-H= 18.7 Hz)


Glycosylation based on P(III) Chemistry
Activator
MS4A, CH2Cl2
X = F
X = (MeO)2PO
α β
Tf2O 76% 11%
Cp2ZrCl2-AgClO4 55 4
Cp2HfCl2-AgClO4 30 10
SnCl2-AgClO4 48 14
NIS-TfOH 76% 14%
ZnCl2-AgClO4 75 24
MeOTf 60 2


NIS, TfOH
CH2Cl2, MS 4A
45%
(β=15%)
TFA
MeOH
TMSOTf
74%
Py-HBr3, Et3N
CH2Cl2, MS 4A
83%
44%
(diastereomer, 45%)
1. EtMgCl 81%
2. C17H35COCl 73%
1. n-Bu4NF-3H2O 89%
PhCOOH
2. PhSH, Et3N 89%
3. H2, Pd-C quant.
PIM2


TeCl4
Ph(CH2)3OH
MS 4A, CH2Cl2
Te
% (α/β)
TeCl4: 91 (97 : 3)
ZnCl2: 83 (51 : 49)
CDCl3
-nBuCl
-TeCl2

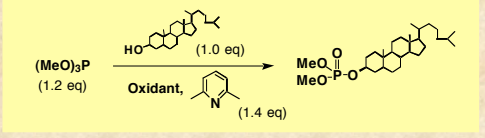


Table 1 酸化剤の検討

Oxidant (eq)	Yield, %
$TeCl_4$ (0.8)	93
$TeBr_4$ (0.8)	76
$Hg(OAc)_2$ (1.2)	90
$Hg(OAc)_2$ (0.8)	64
$FeCl_3$ (1.2)	37
$HgCl_2$ (0.8)	6
$CuCl_2$ (0.8)	---
$Pb(OAc)_4$ (0.8)	---

Solv: CH_2Cl_2

Table 2 当量の検討

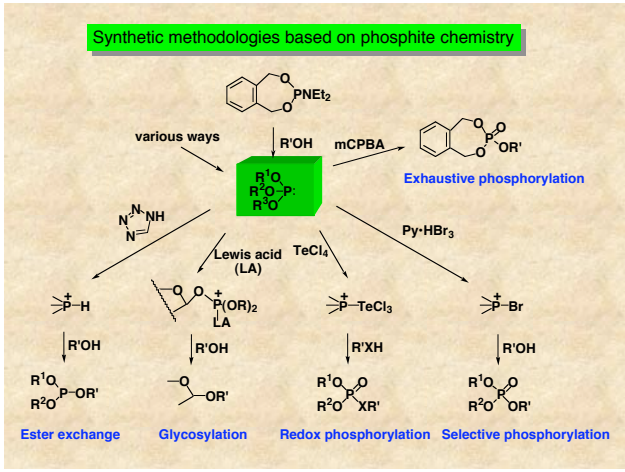
Equiv of $TeCl_4$	Yield, %
0.4	53
0.5	80
0.6	89
0.7	90
0.8	93
0.9	86
1.0	85
1.1	86
1.4	84
1.8	75

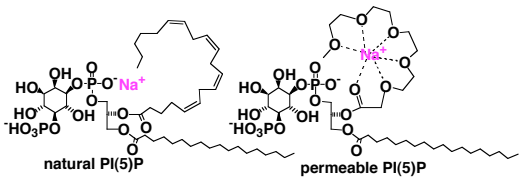
Solv: CH_2Cl_2

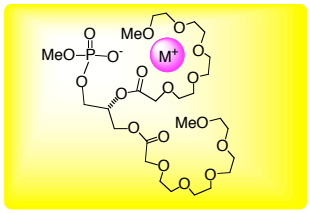
Table 3 溶媒の検討

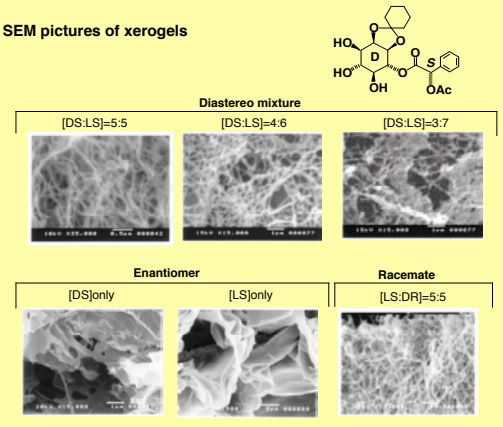
Solvent	Yield, %
CH_2Cl_2	93
Benzene	73
THF	64
CH_3CN *	50
Et_2O	44

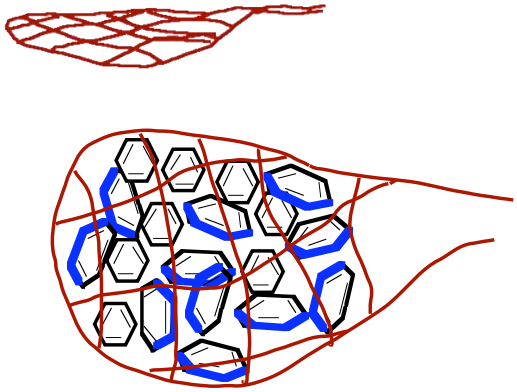
*$Ph(CH_2)_3OH$ used



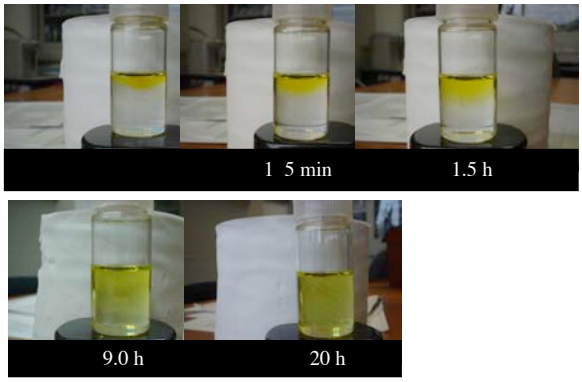


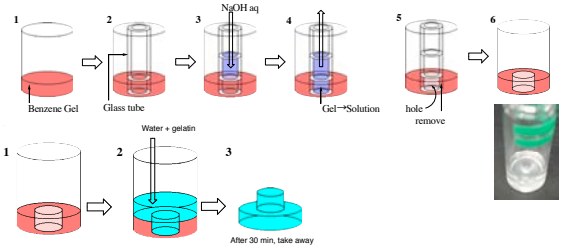




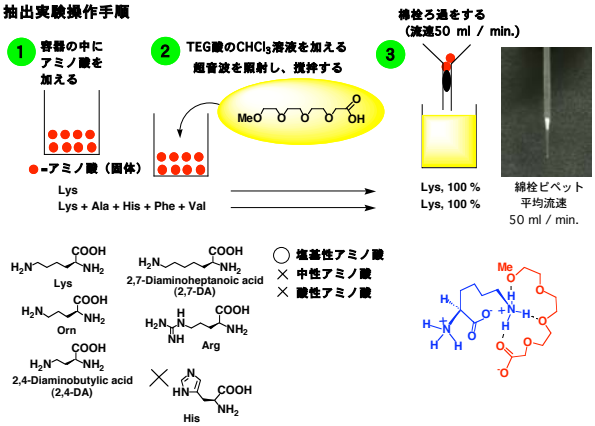


ベンゼンゲル内の色素の拡散速度





抽出実験操作手順



Lysの当量数と抽出量の関係