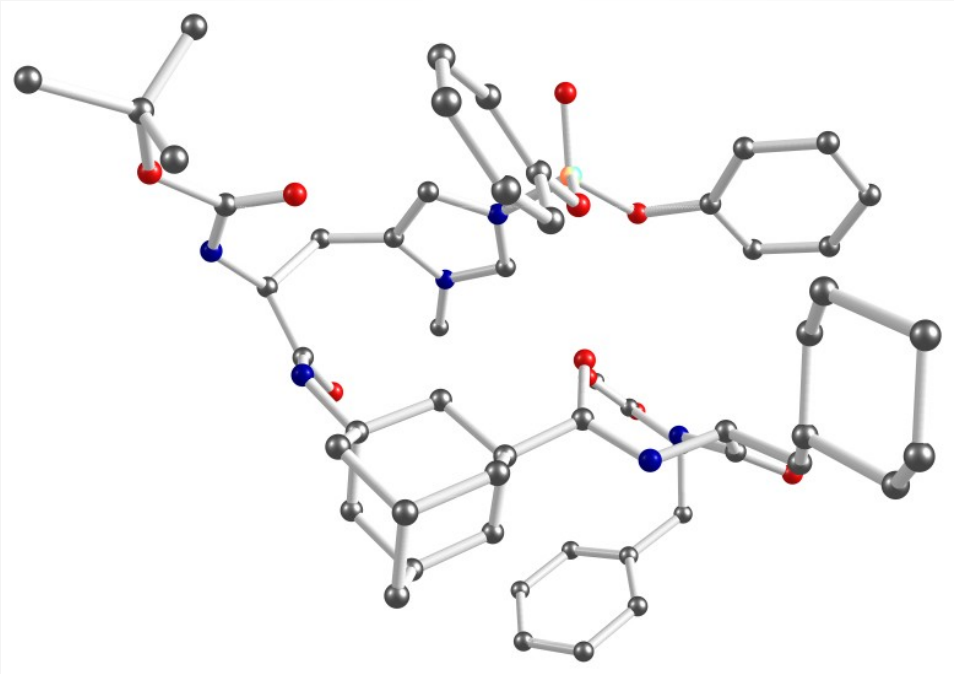
Organocatalytic transfer of electrophiles mediated by short Peptides



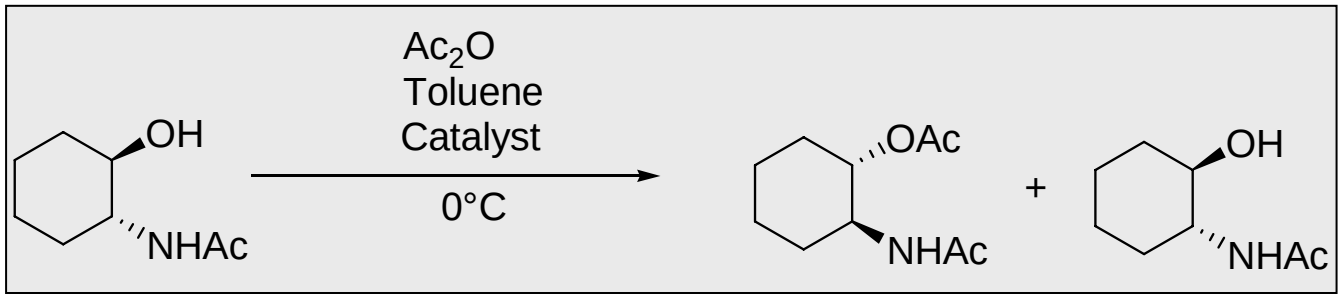
Daniela Zell 06.02.2009

Content:

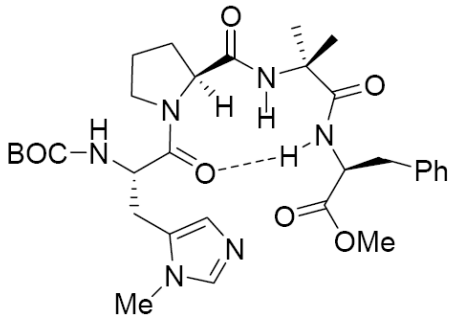
1. Indroduction
2. Phosphoryl transfer
3. Sulfonyl transfer
4. *Tert*-butoxycarbonyl transfer
5. Outlook

1.Introduction

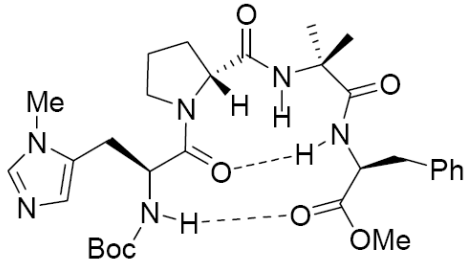
Kinetic resolution of *trans*-1,2-acetamidocyclohexanol by Miller et al.



k(S.S)/k(R.R) = 3,1;
conversion = 56%;
ee = 51%



L-Pro



D-Pro

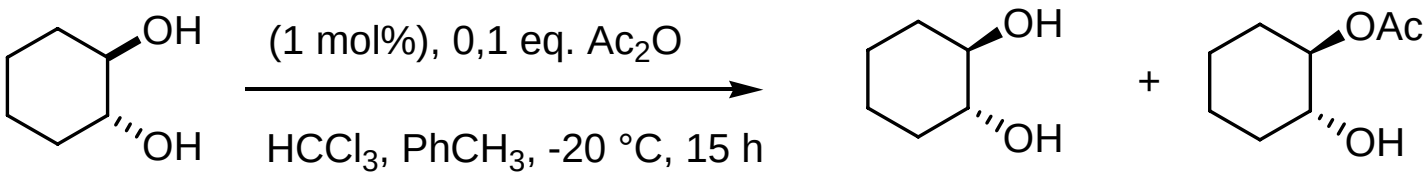
k(R.R)/k(S.S) = 28;
conversion = 58%;
ee = 93%

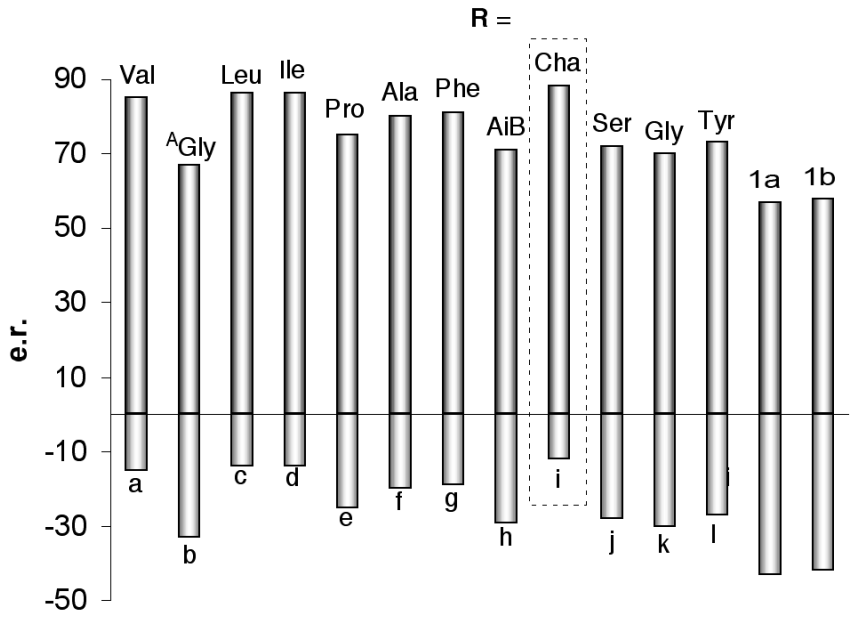
E. A. C. Davie, S. M. Mennen, Y. Xu, S. J. Miller, *Chem. Rev.* **2007**, *107*, 5759.

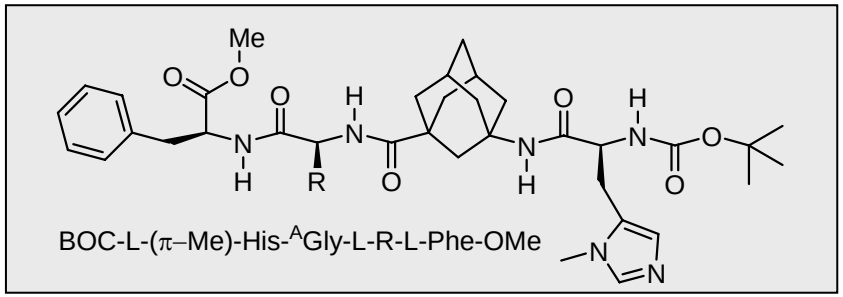
E. R. Jarvo, G. T. Copeland, N. Papaioannou, P. J. Bonitatebus, S. J. Miller, *J. Am. Chem. Soc.* **1999**, *121*, 11638.

E. R. Jarvo, S. J. Miller, *Tetrahedron* **2002**, *58*, 2481.

Enantioselective kinetic resolution of *trans*-cyclohexan-1,2-diol



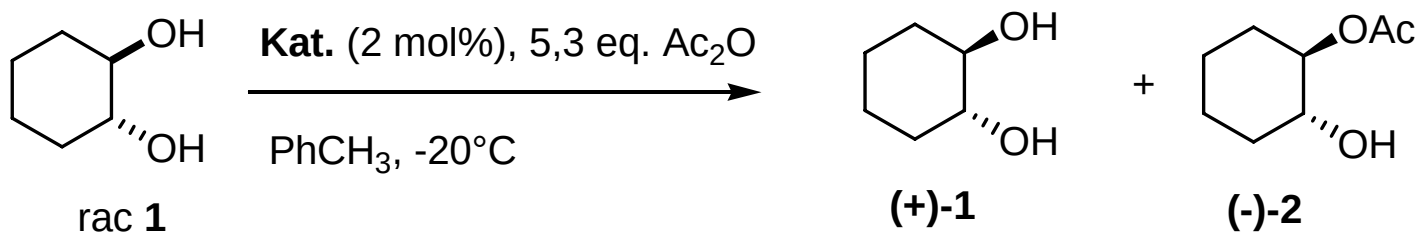




Catalyst screening for enantioselective acylation test reaction.

C. E. Müller, L. Wanka, K. Jewell, P. R. Schreiner, *Angew. Chem.* **2008**, *120*, 6275**.**

Enantioselective kinetic resolution of *trans*-cyclohexan-1,2-diol



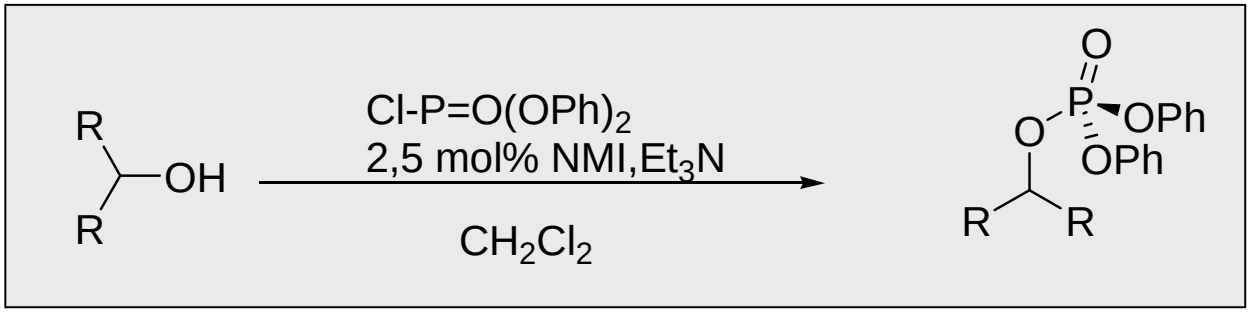
Entry	t [h]	Conv. [%][a]	ee [%] (+)-1	ee [%] (-)-2	s-factor [a]
1	1	29	37	91	30
2	3	49	92	85	34
3	4	55	99	80	>50

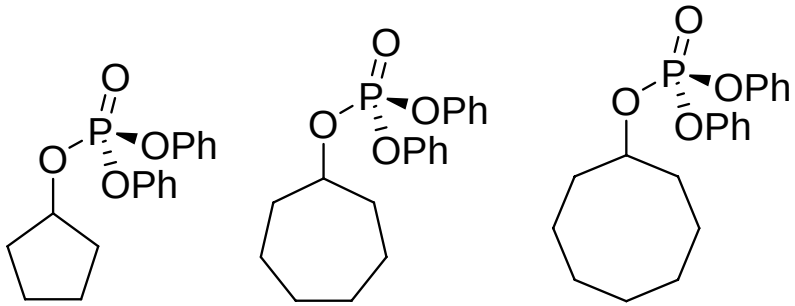
[a] Conversion and s-factors determined following the procedure of Kagan and Fiaud.

H. B. Kagan, J. C. Fiaud, *Top. Stereochem* **1988**, *18*, 249.

2. Phosphoryl Transfer

Amin-based catalysis of alcohol phosphorylation.

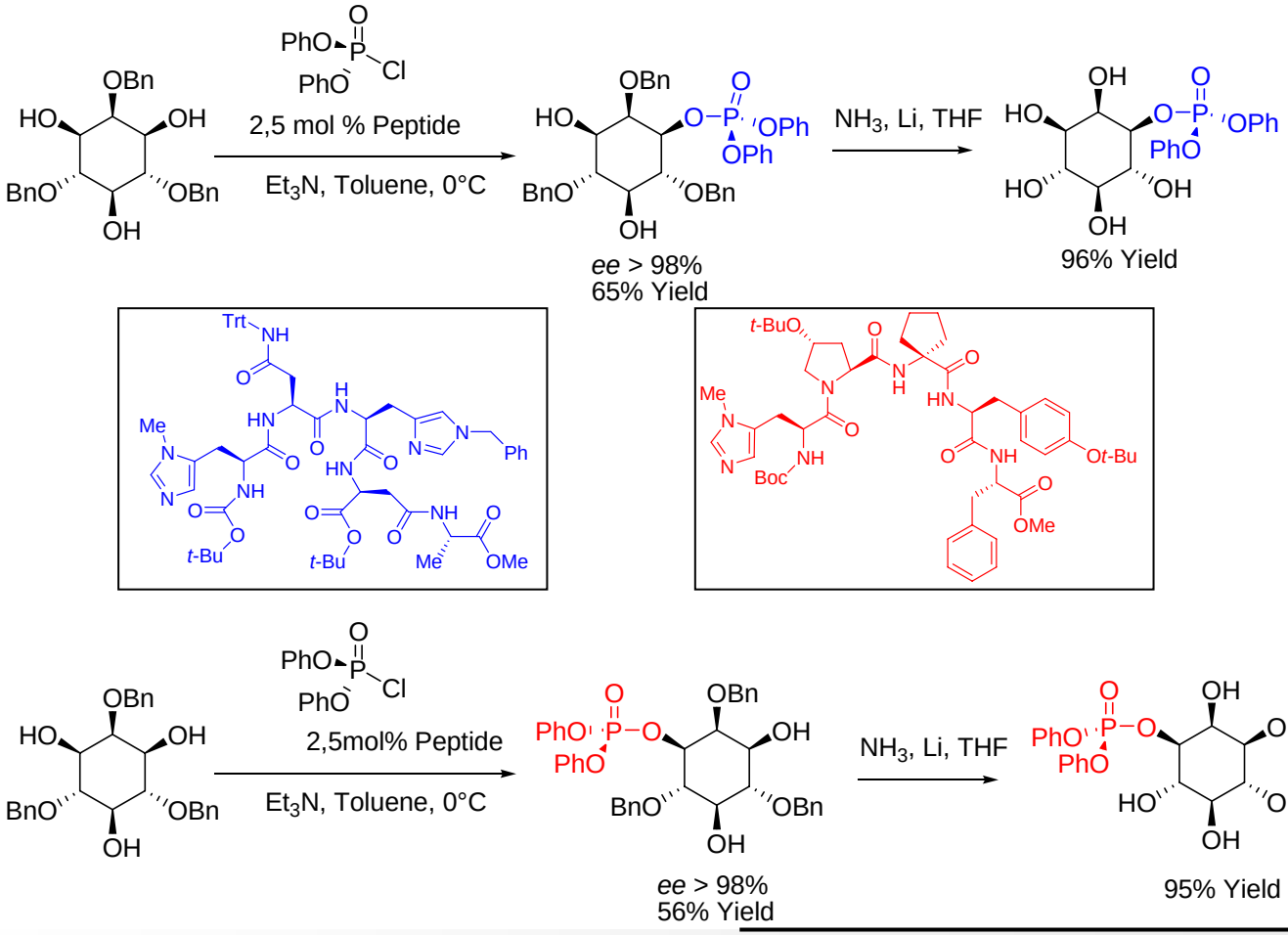




Yield : 95% 86% 66%

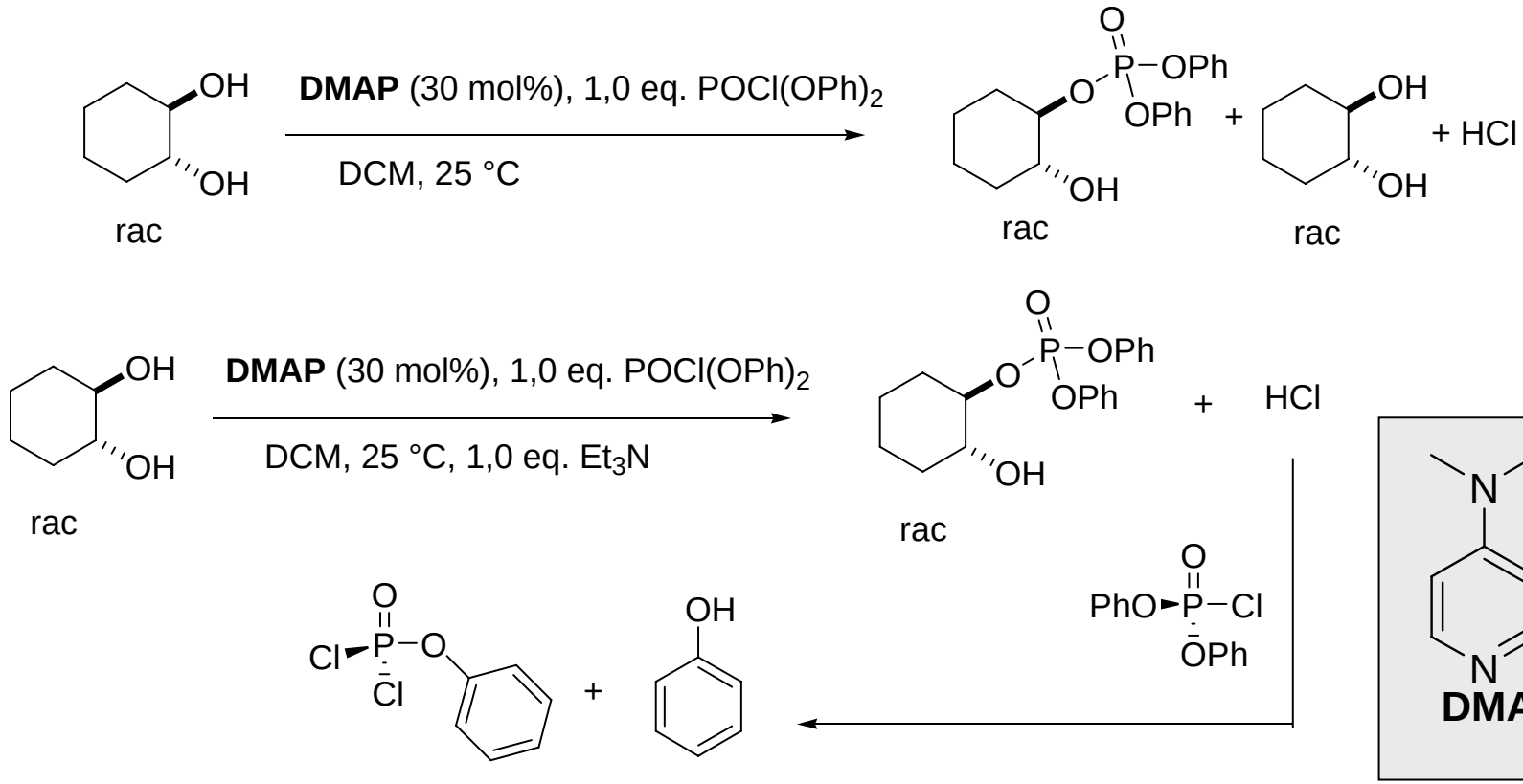
B. R. Sculimbrene, S. J. Miller, *J. Am. Chem. Soc.* **2001**, *123*, 10125.

Desymmetrization of *myo*-inositol-derivative mediated by pentapeptides

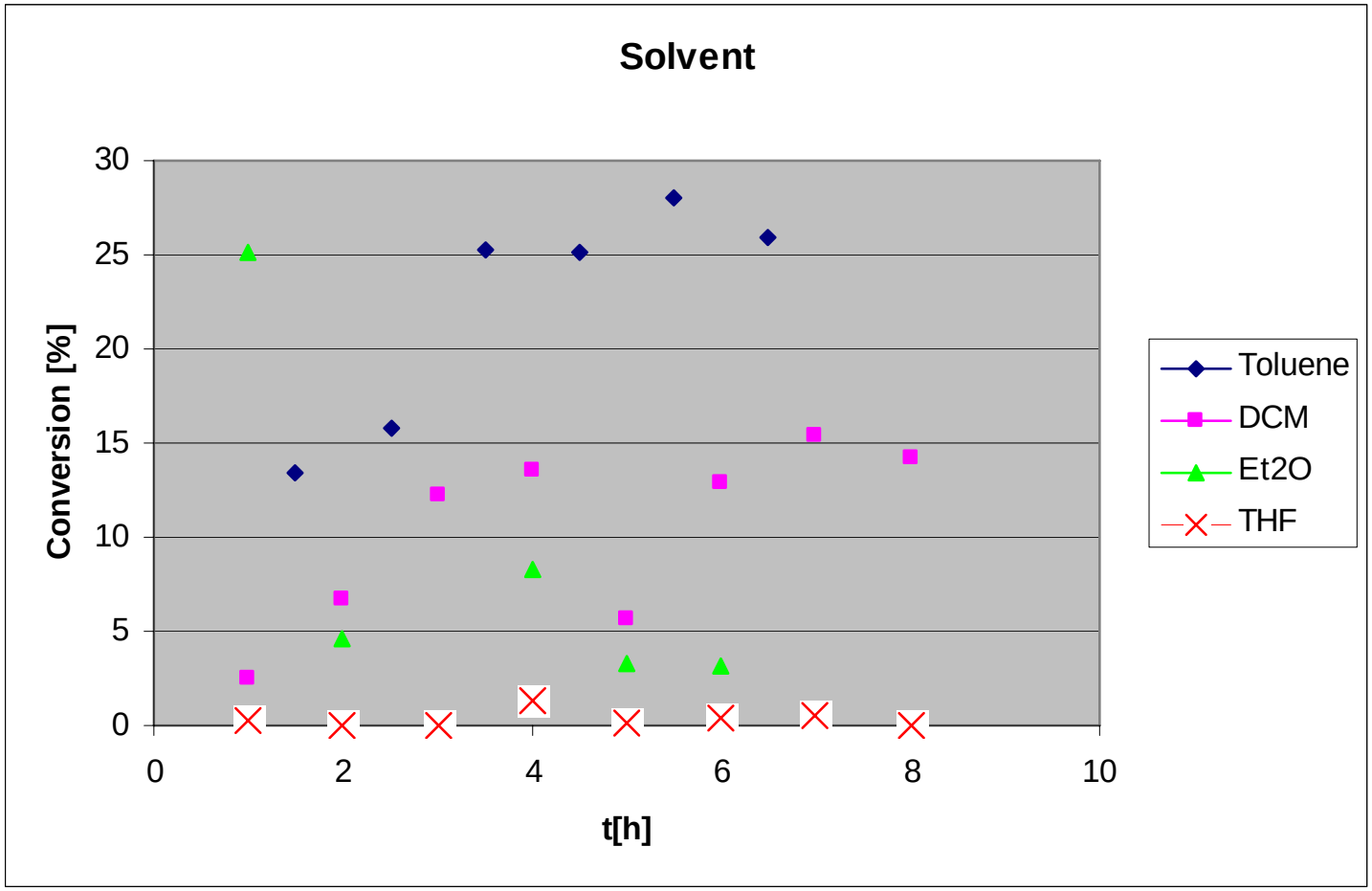


[1] E. A. C. Davie, S. M. Mennen, Y. Xu, S. J. Miller, *Chem. Rev.* **2007**, *107*, 5759;
[2] S. J. Miller, *Acc. Chem. Res* **2004**, *37*, 601; [3] E. R. Jarvo, S. J. Miller, *Tetrahedron* **2002**, *58*, 2481.
[4] B. R. Sculimbrene, A. J. Morgan, S. J. Miller, *J. Am. Chem. Soc.* **2002**, *124*, 11653.
[5] A. J. M. Bianca R. Sculimbrene, Scott J. Miller, *Chem. Commun.* **2003**, 1781.

DMAP catalyzed phosphorylation test reaction



Optimization of the reaction conditions



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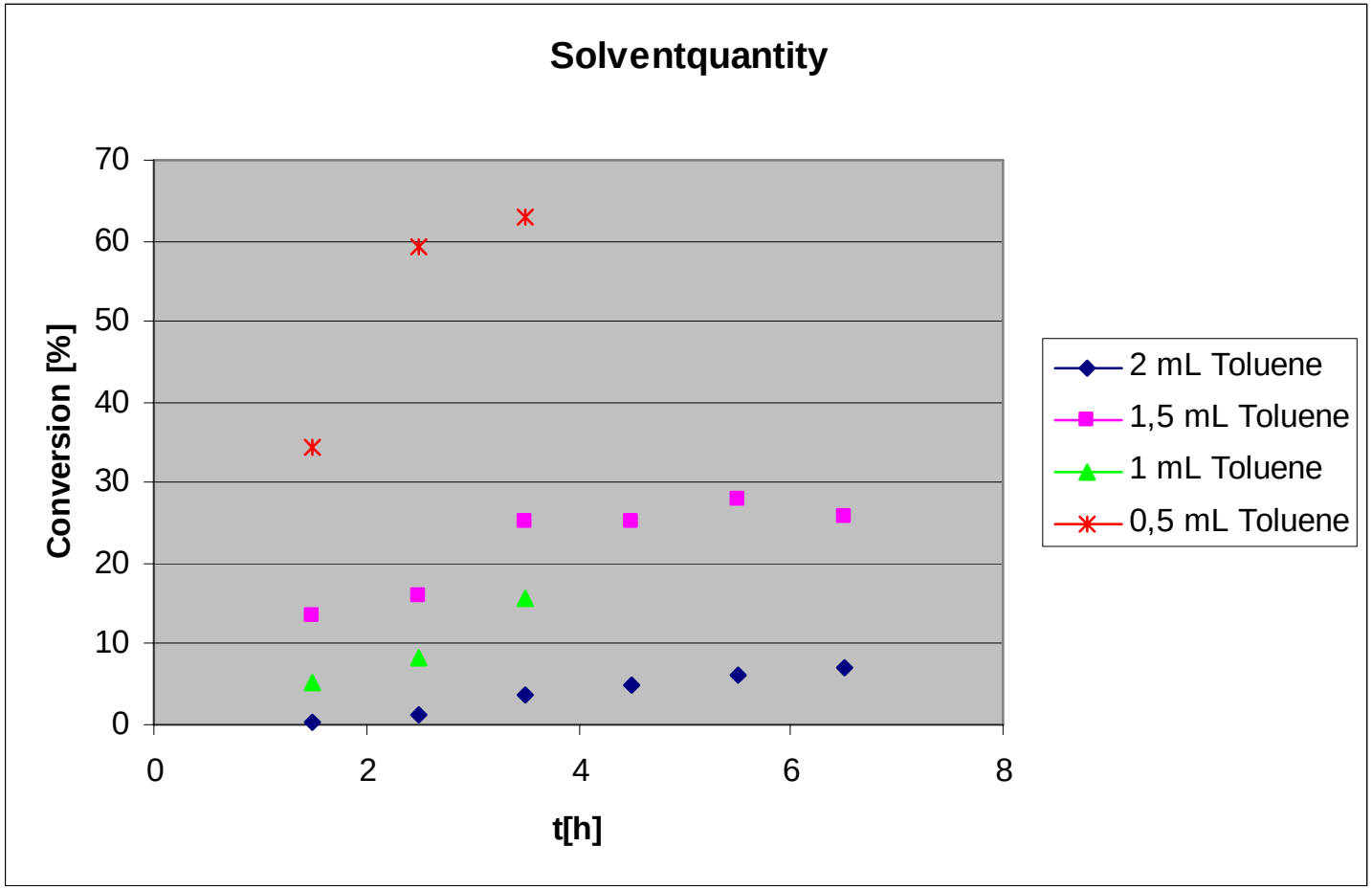
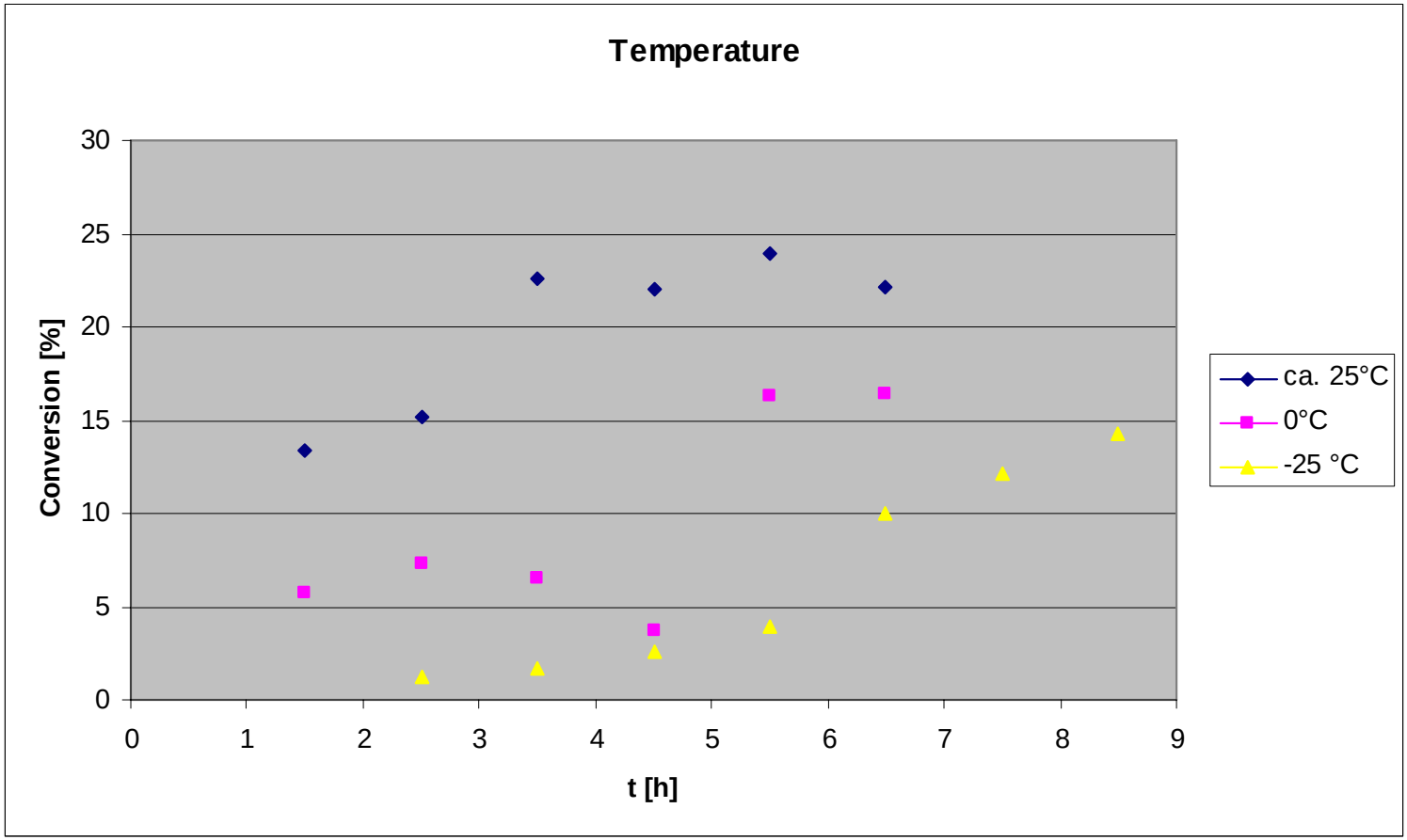
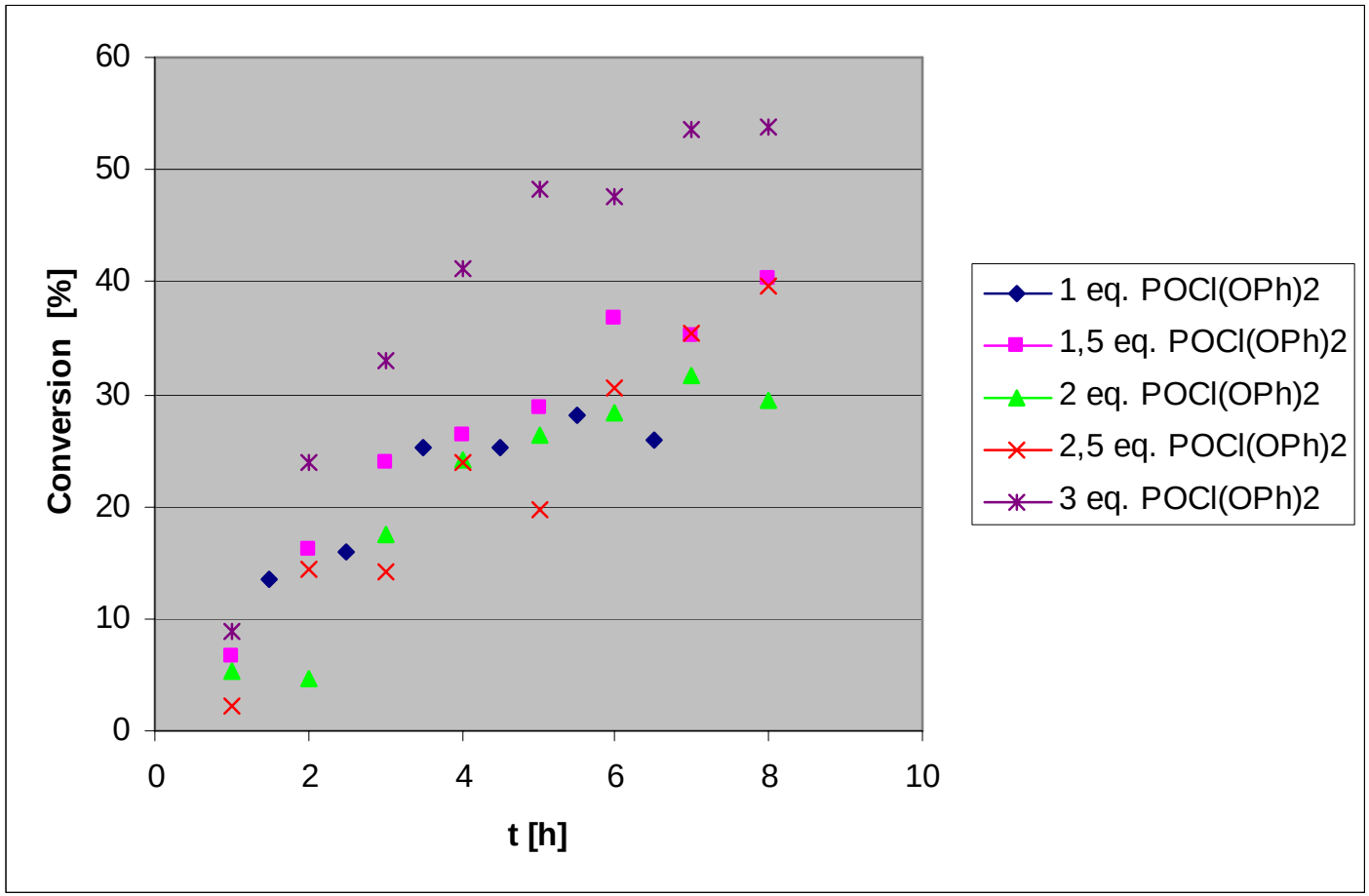


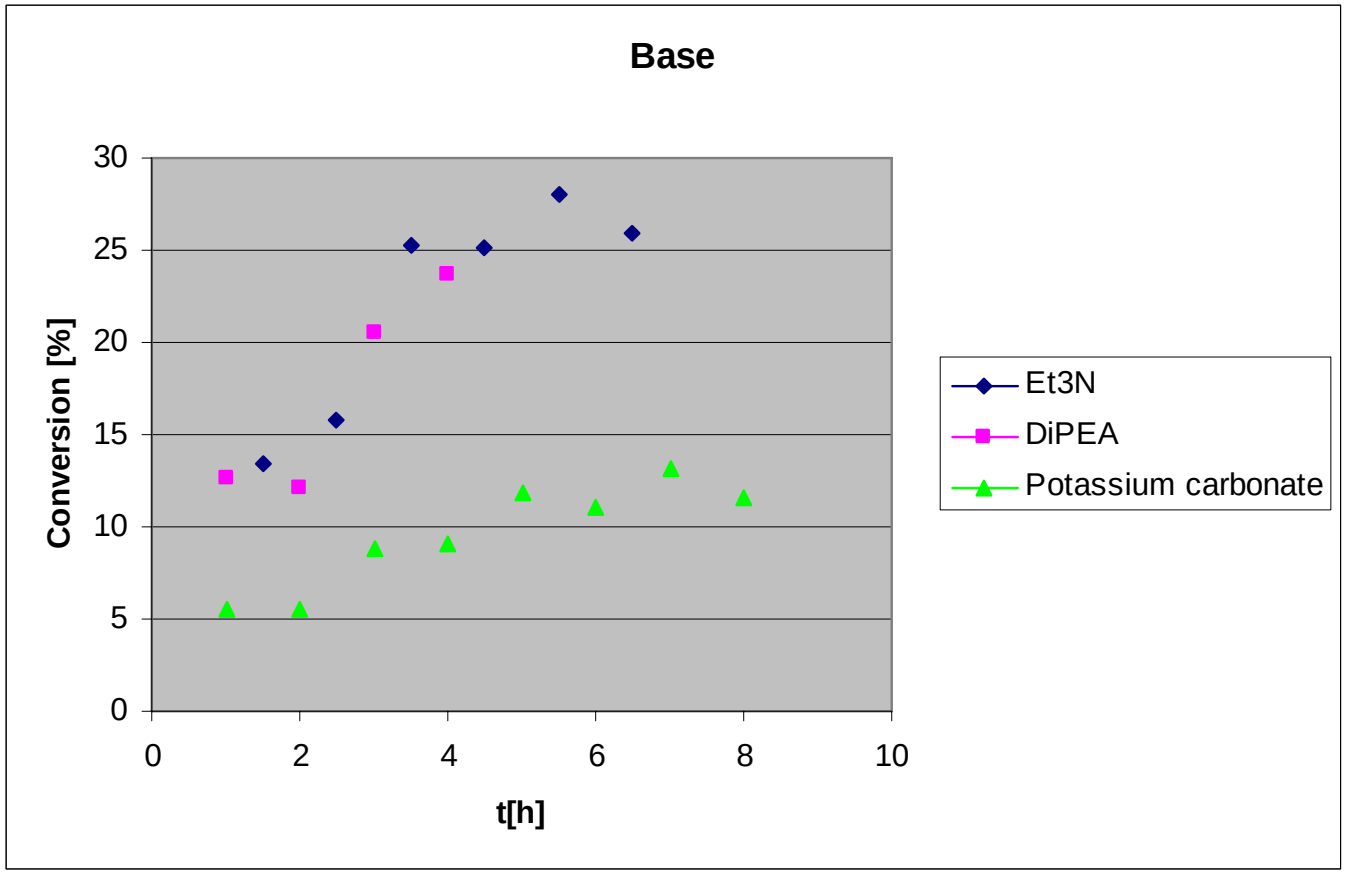
Optimization of the reaction conditions



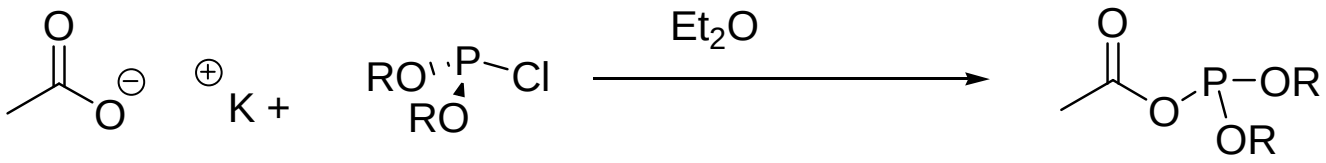
Optimization of the reaction conditions

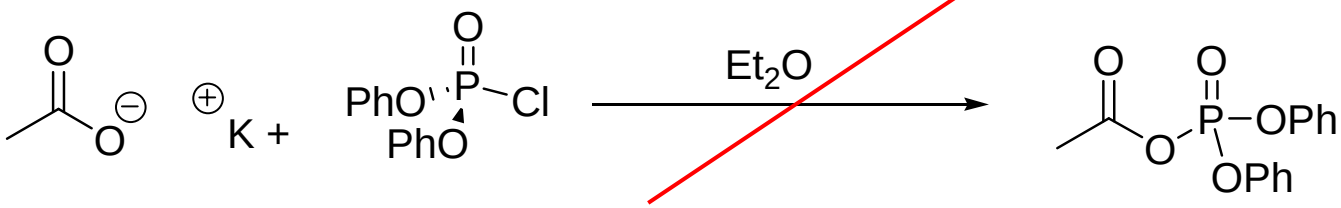


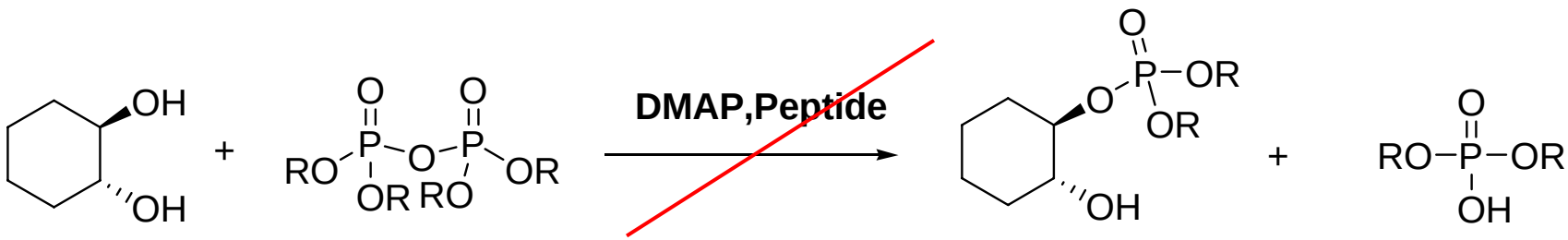
Optimization of the reaction conditions



Alternative phosphorylation reagent



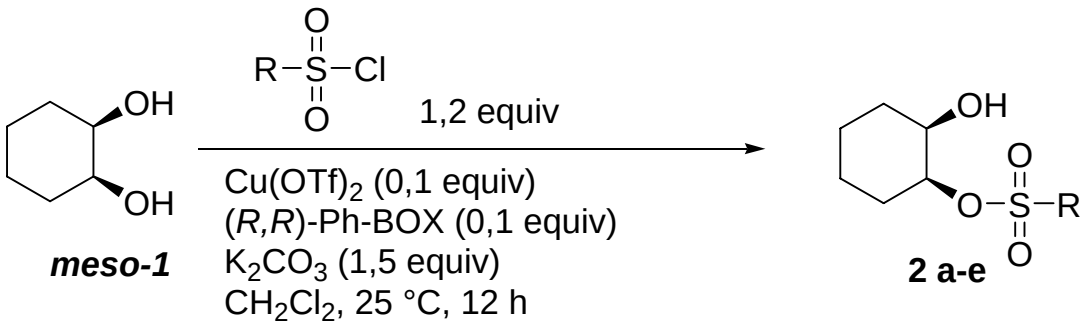


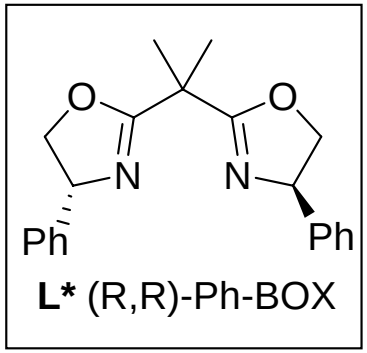


K. A. Petrov, E. E. Nifantév, I. I. Sopikova, U. M. Budanov, *International Patent SU13548719610215* **1961**.

3.Sulfonyl Transfer

Asymmetric monosulfonylation of *meso*-*vic*-diols

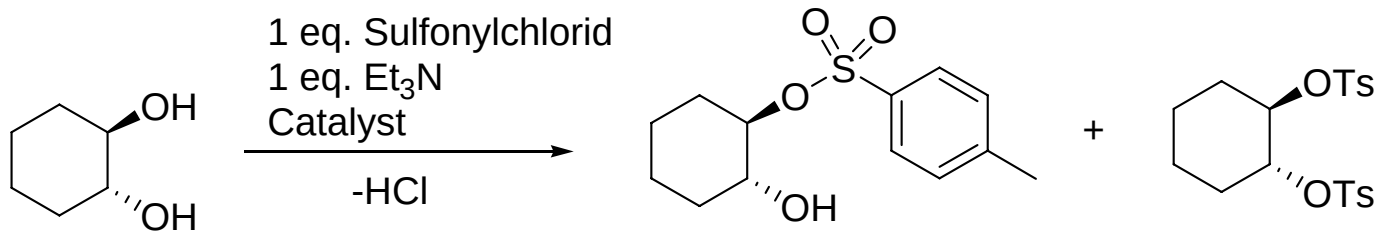




Entry	R	Product	Yield [%]	*ee* [%]
1	a: Ph	2a	91	98
2	b: *p*-NO_2-Ph	2b	59	92
3	c: *p*-ClPh	2c	93	93
4	d: *p*-MeOPh	2d	61	94
5	e: Me	2e	93	77

Y. Demizu, K. Matsumoto, O. Onomura, Y. Matsumura, *Tetrahedron Lett.* **2007**, *48*, 7605.

Kinetic resolution of *trans*-Cyclohexane-1,2-diol using sulfonylchlorides as electrophiles

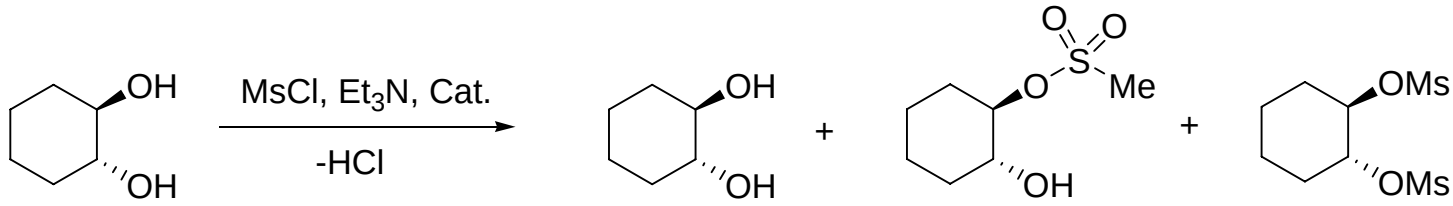


1 **2** **3**

Entry	Cat.	time [h]	solvent	base	Yield 2 [%]
1	DMAP[a]	8	Toluene	Et3N	-
2	Peptide[b]	8	Toluene	Et3N	-
3	-	8	Toluene	Et3N	-
4	DMAP	12	DCM	Et_3N	-
5	DMAP	12	DCM	K_2CO_3	-

[a] 30 mol%; [b] 5 mol%

Kinetic resolution of *trans*-Cyclohexane-1,2-diol using sulfonylchlorides as electrophiles

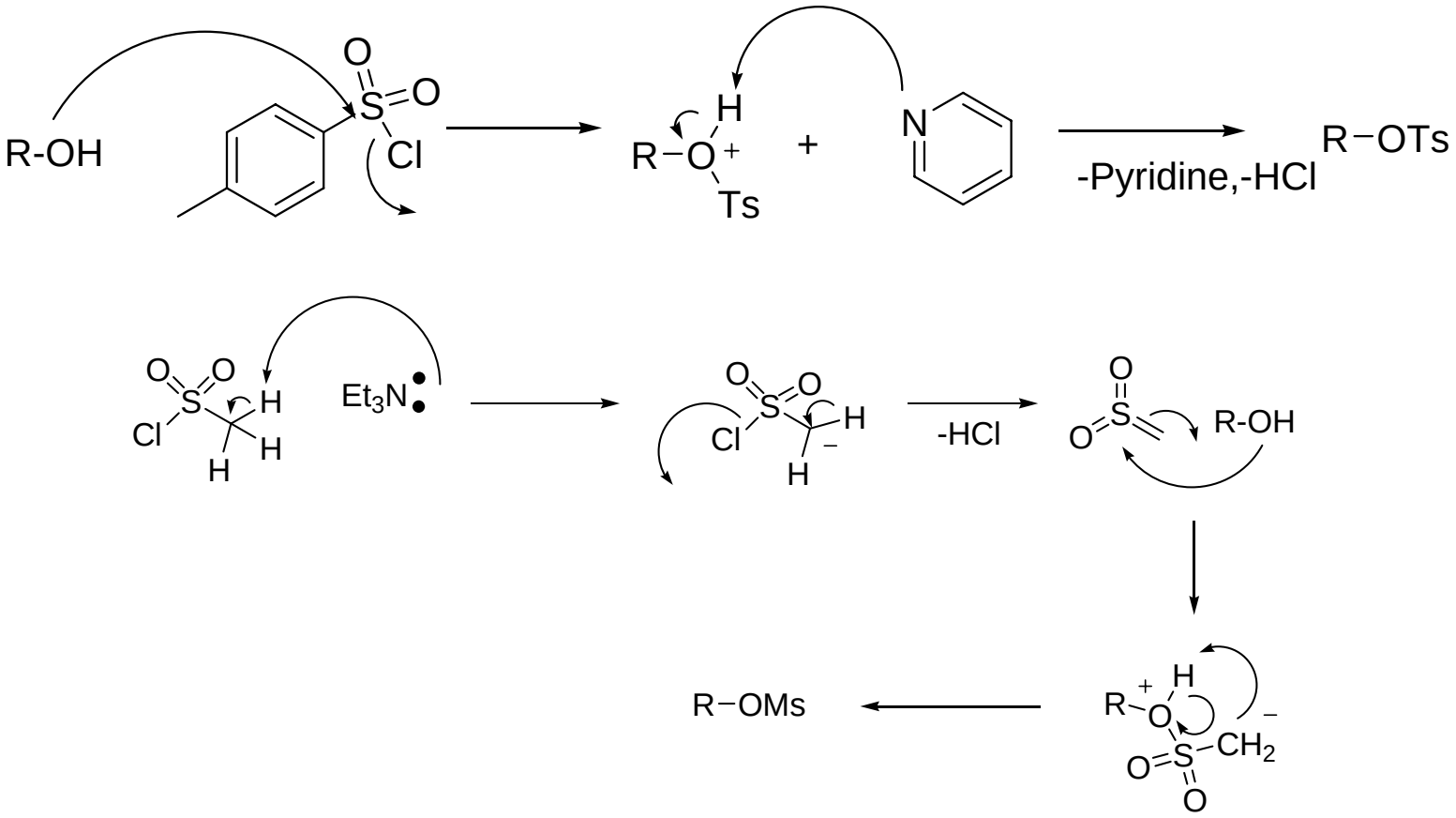


(+/-)-1 **(+/-)-1** **2** **3**

Entry	Cat.	time [h]	solvent	Yield 2 [%]	Yield 3 [%]
1	DMAP[a]	24	Toluene	2	83
2	Peptide[b]	24	Toluene	40	60
3	-	24	Toluene	45	30

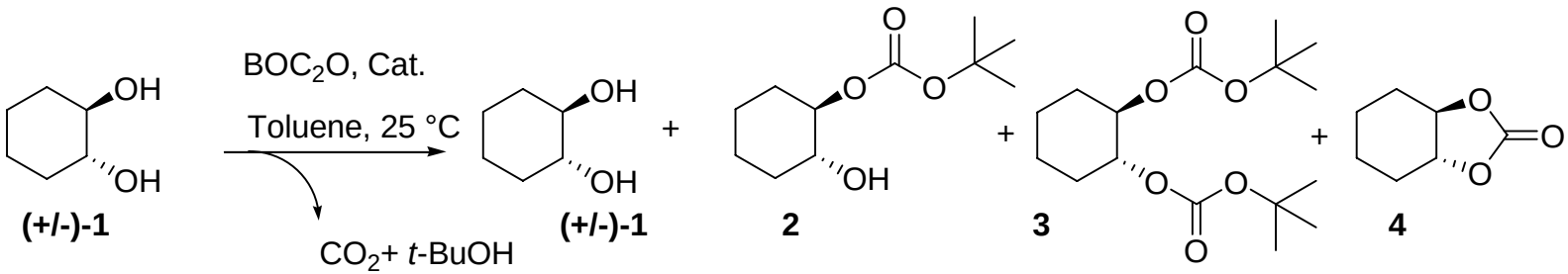
[a] 30 mol%; [b] 5 mol%

Tosylation mechanism versus Mesylation mechanism

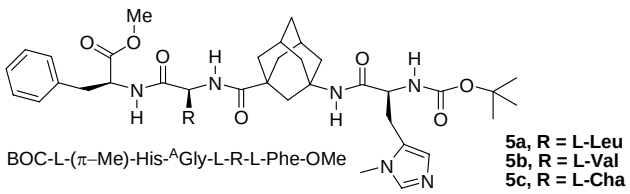


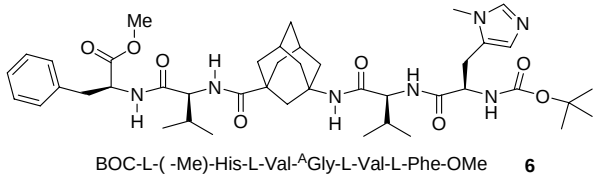
J. F. King, J. R. du Manoir, *J. Am. Chem. Soc.* **1975**, *97*, 2566.

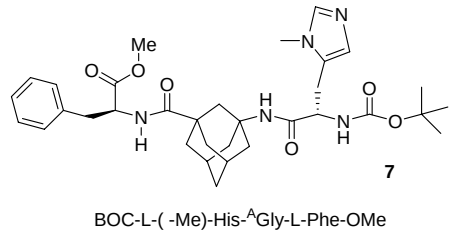
4.Tert-butoxycarbonyl Transfer



Entry	Cat.	time [h]	conversion 2 [%]	*ee* 1 [%]	*ee* 2 [%]	s-factor
1	5a	9	38	26	42	3,1
2	5b	9	32	18	39	2,7
3	5c	9	28	16	42	2,9
4	6	9	12	2	15	1,4
5	7	9	27	9	24	1,8



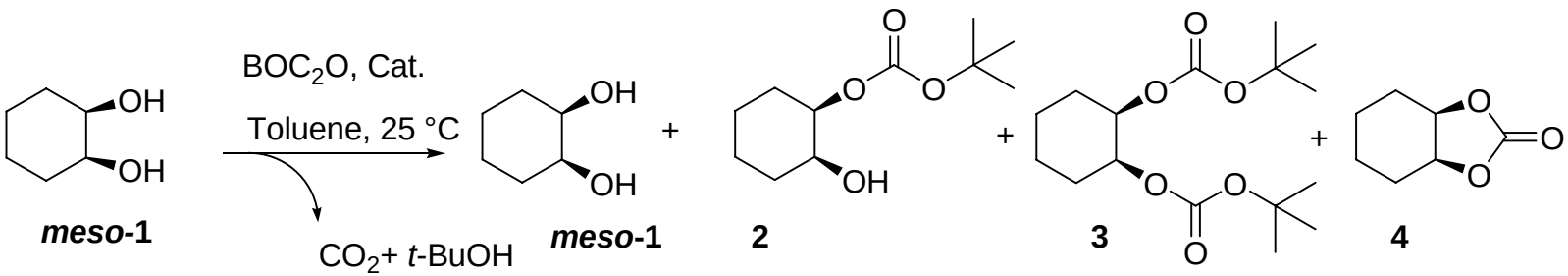




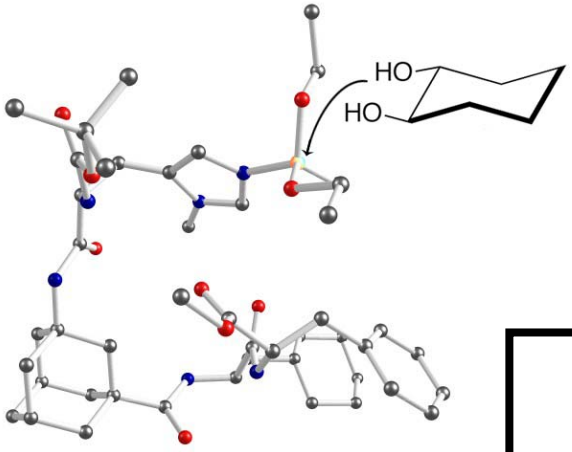
Y. Basel, A. Hassner, *J. Org. Chem.* **2000**, *65*, 6368.

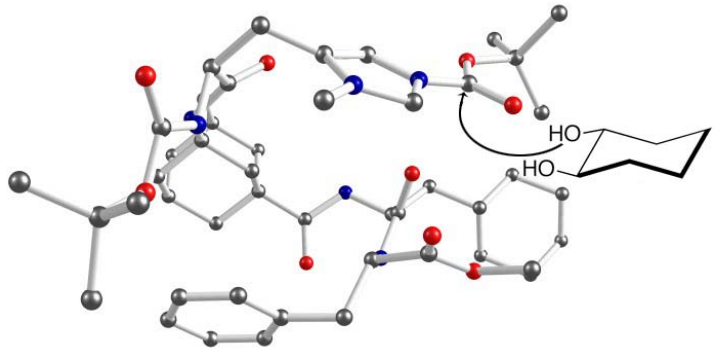
H. B. Kagan, J. C. Fiaud, *Top. Stereochem* **1988**, *18*, 249.

Tert-butoxycarbonyl transfer



Entry	Cat.	time [h]	conv. 2 [%]	conv.3 [%]	conv. 4 [%]
1	DMAP	12	77	9	14
2	5a	12	-	-	24
3	5a	24	20,4	-	21,6
4	5a	48	20,2	-	47,8
5	5a	120	53,4	-	40,4


HO
HO


HO
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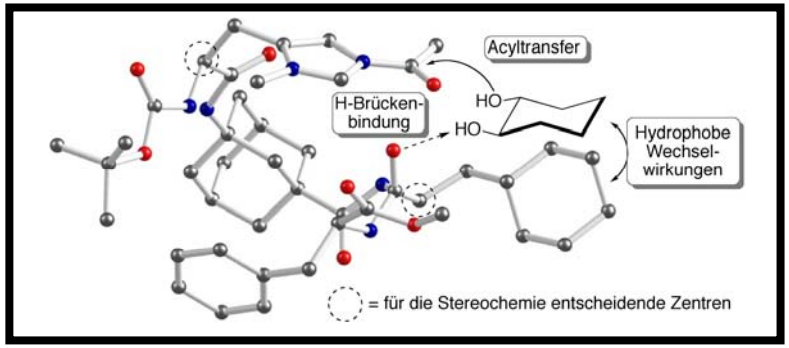
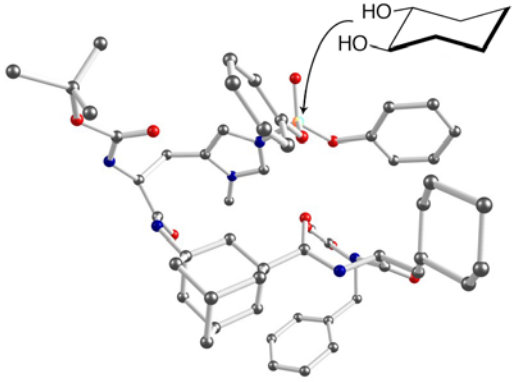
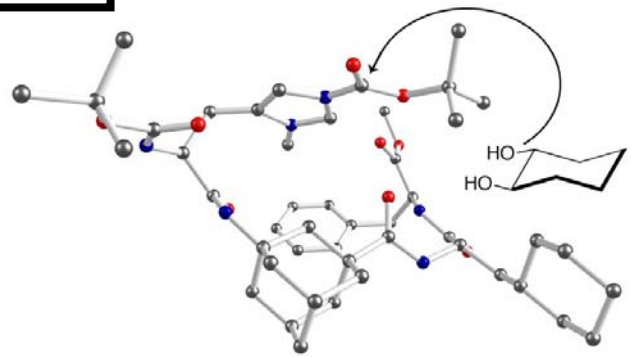
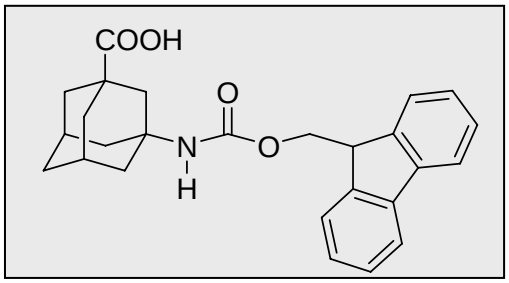
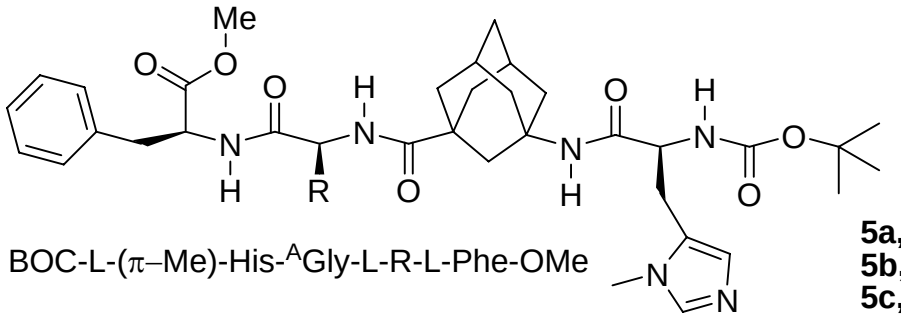

Acyltransfer
H-Brücken-
bindung
HO
HO
Hydrophobe
Wechsel-
wirkungen
= für die Stereochemie entscheidende Zentren


HO
HO


HO
HO

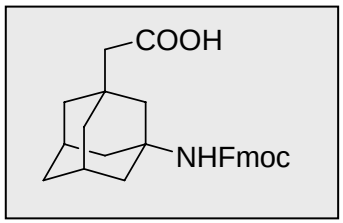
5.Outlook

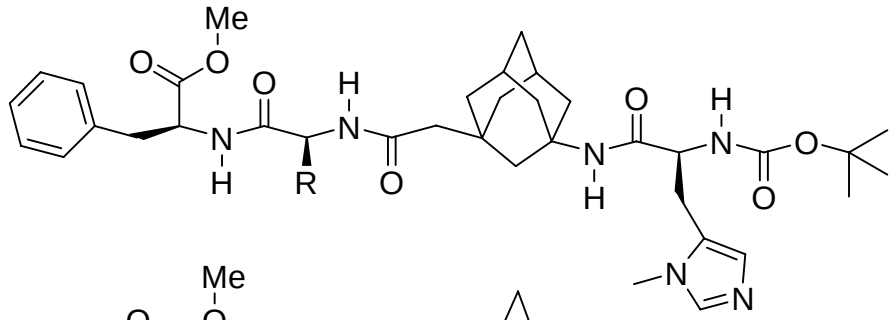


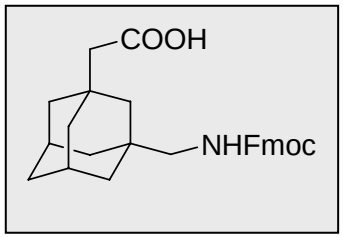


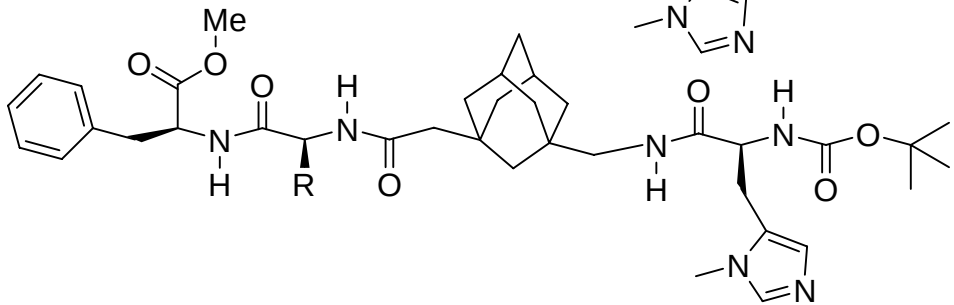
BOC-L-(π–Me)-His-^{A}Gly-L-R-L-Phe-OMe

5a, R = L-Leu
5b, R = L-Val
5c, R = L-Cha

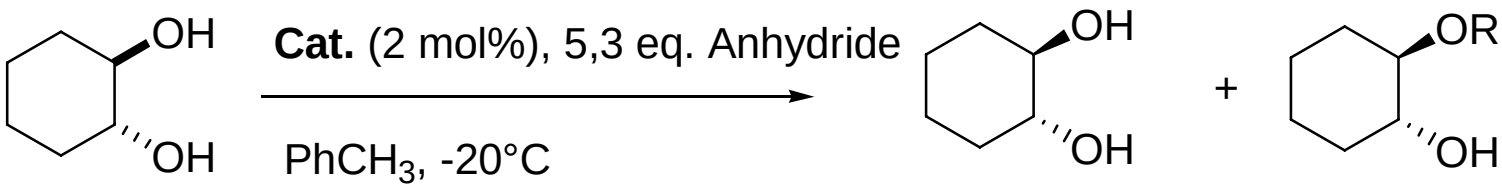


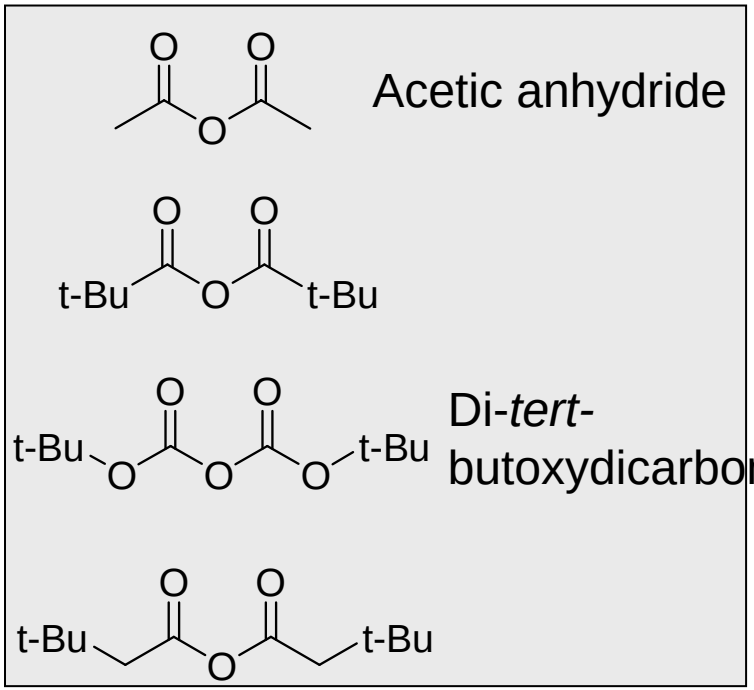






Outlook





Checking the influences of electronic and steric effects on the reaction rate and the stereospecifity.