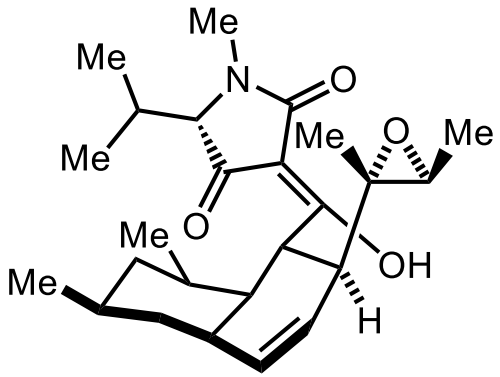
WILEY-VCH

COMMUNICATION

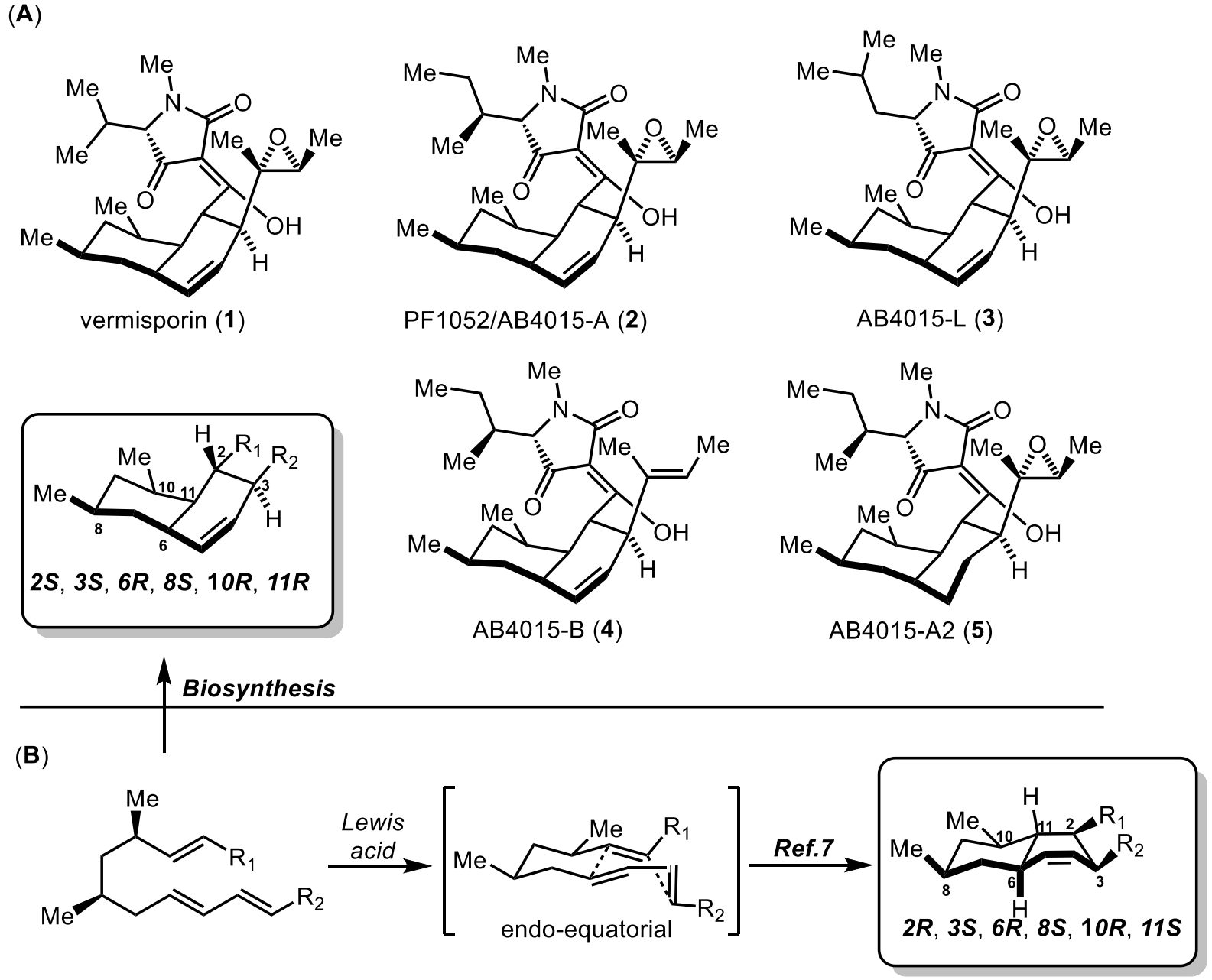
Total Synthesis of Diverse Tetramic Acid Bearing *cis*-Decalin Natural Products

Haoran Dong,[a] ‡ Dachao Hu,[b] ‡ Benke Hong,[a] ‡ Jin Wang,[a] Xiaoguang Lei*[a,c]

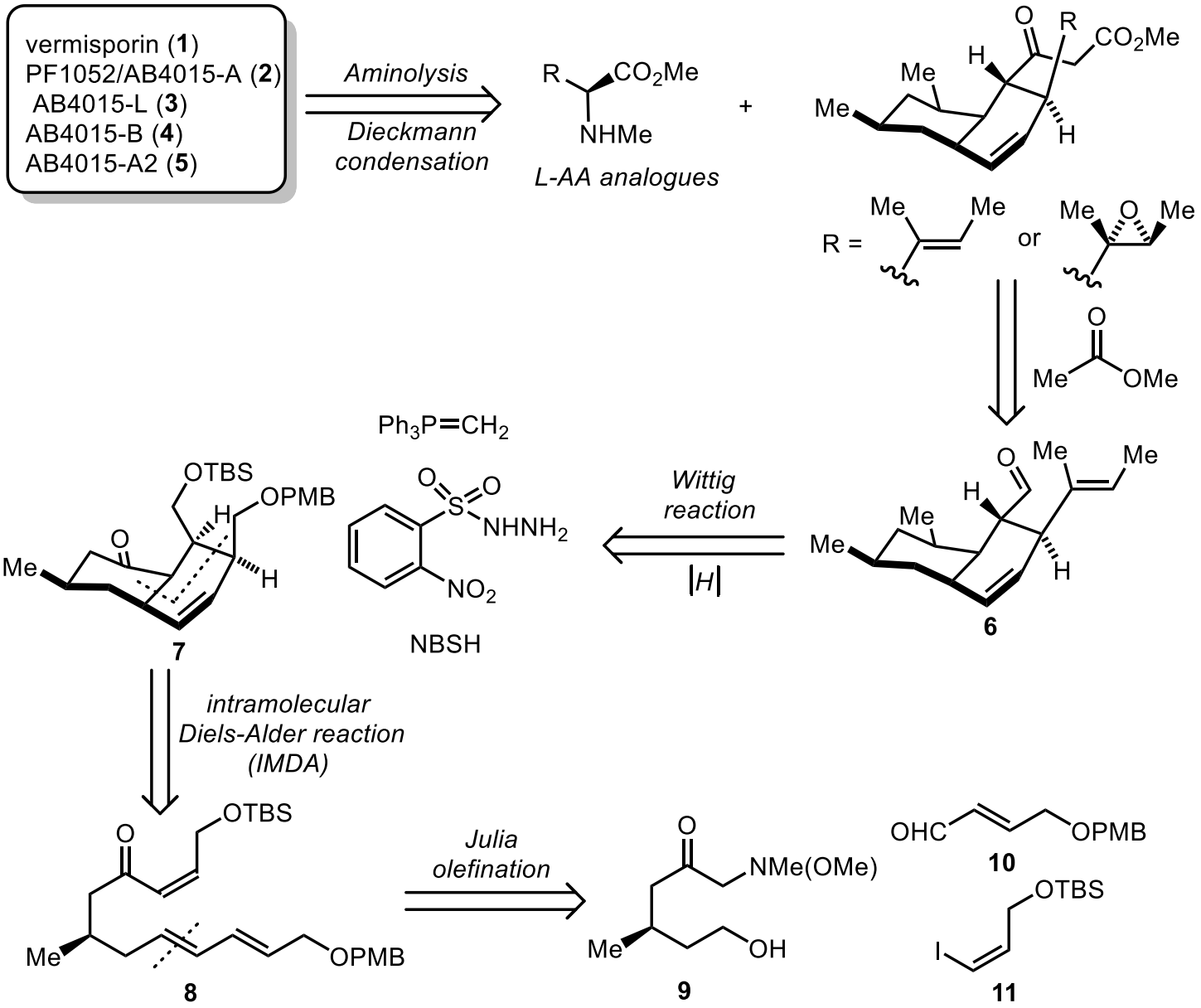


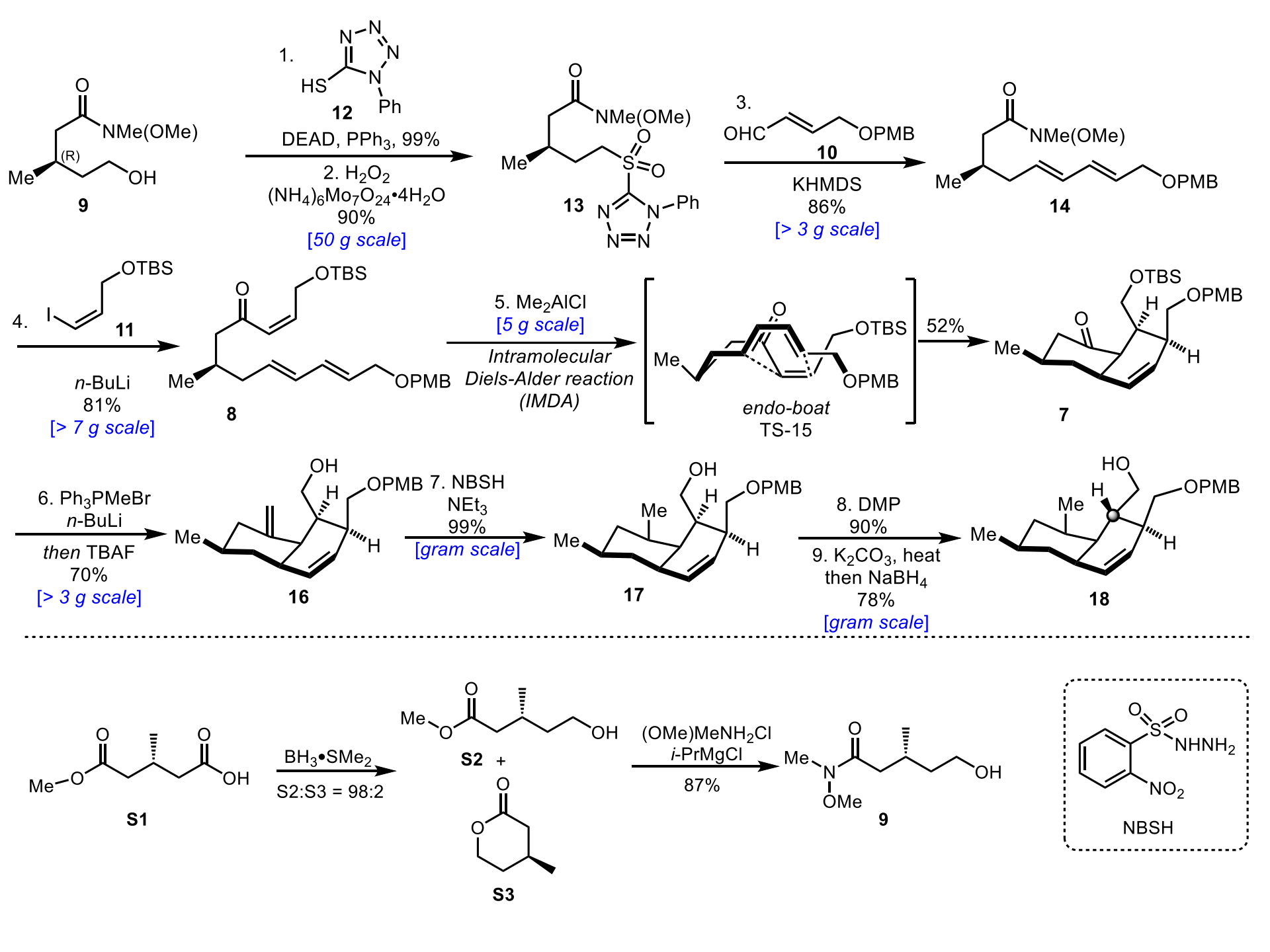
vermisporin (**1**)

Angew. Chem. Int. Ed., **2023**, e202301872.


(A)
vermisporin (1)
PF1052/AB4015-A (2)
AB4015-L (3)
2S, 3S, 6R, 8S, 10R, 11R
AB4015-B (4)
AB4015-A2 (5)
Biosynthesis
(B)
Lewis acid
endo-equatorial
Ref.7
2R, 3S, 6R, 8S, 10R, 11S

Retrosynthetic analysis

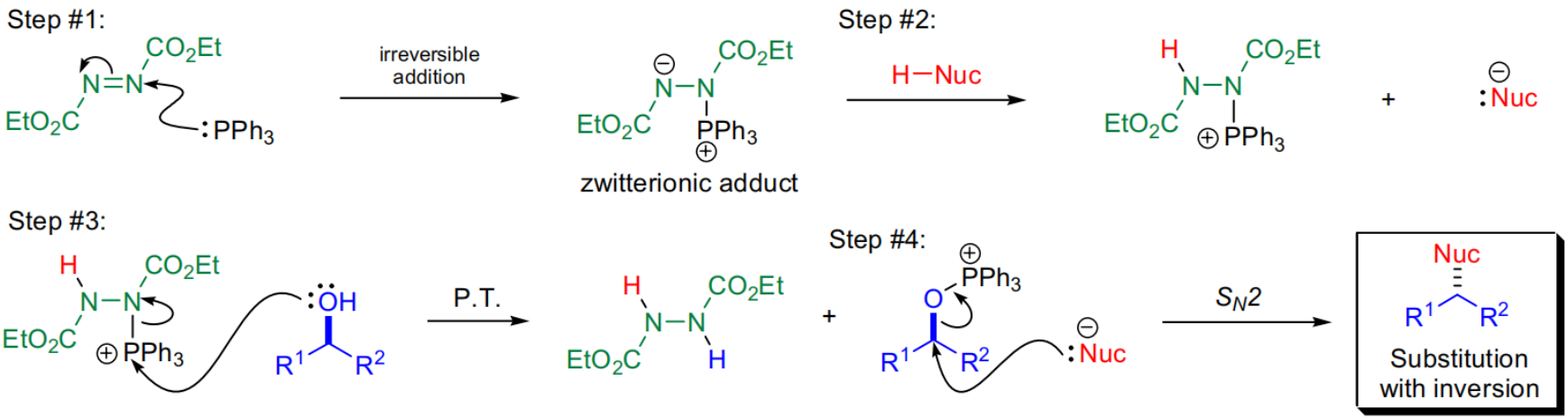



1.
12
DEAD, PPh3, 99%
2. H2O2
(NH4)6Mo7O24•4H2O
90%
[50 g scale]
9
13
3.
10
KHMDS
86%
[> 3 g scale]
14
4.
11
n-BuLi
81%
[> 7 g scale]
8
5. Me2AlCl
[5 g scale]
Intramolecular
Diels-Alder reaction
(IMDA)
endo-boat
TS-15
52%
7
6. Ph3PMeBr
n-BuLi
then TBAF
70%
[> 3 g scale]
16
7. NBSH
NEt3
99%
[gram scale]
17
8. DMP
90%
9. K2CO3, heat
then NaBH4
78%
[gram scale]
18
S1
BH3•SMe2
S2:S3 = 98:2
S2
+
S3
(OMe)MeNH2Cl
i-PrMgCl
87%
9
NBSH

MITSUNOBU REACTION

(References are on page 632)

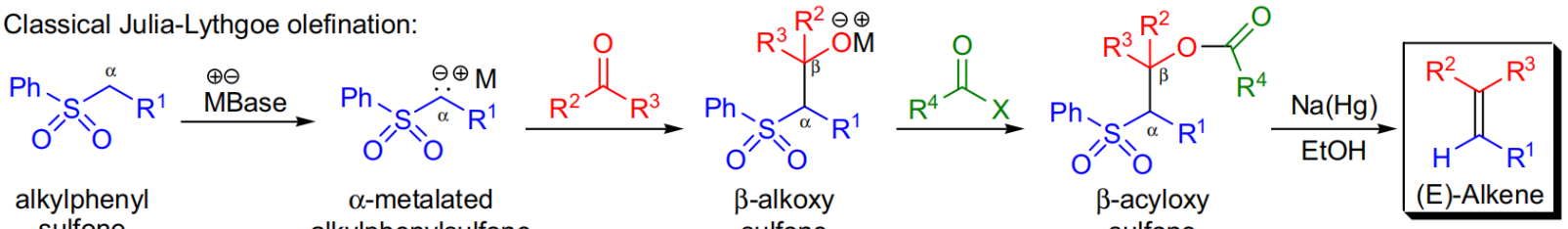
Mechanism: [25-45]



JULIA-LYTHGOE OLEFINATION

(References are on page 610)

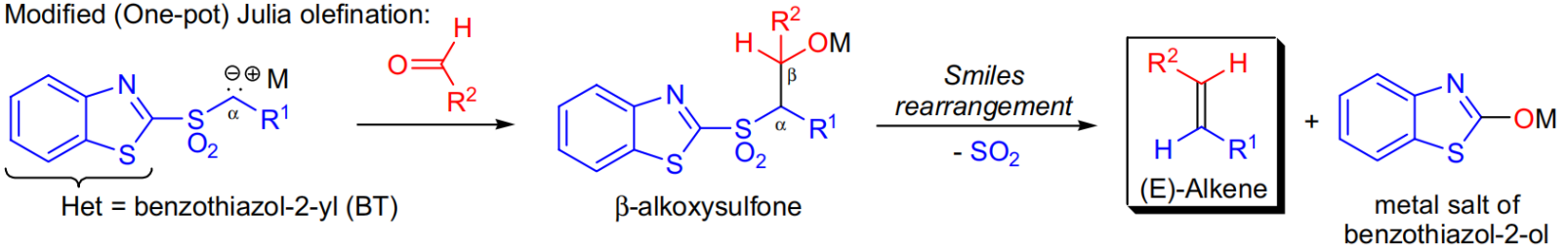
Classical Julia-Lythgoe olefination:



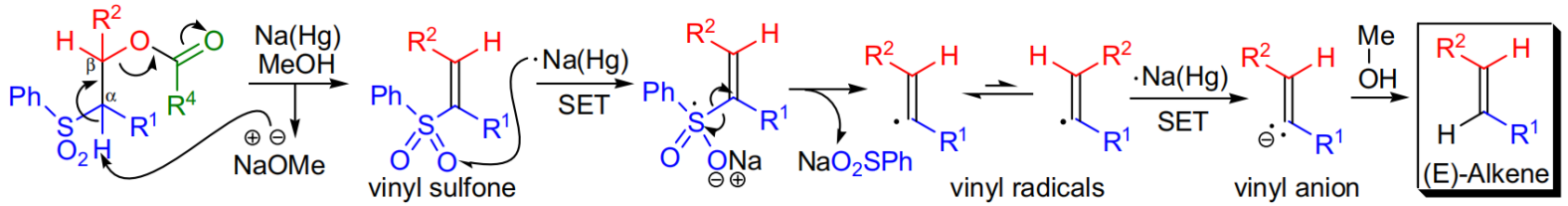
alkylphenyl sulfone | α-metalated alkylphenylsulfone | β-alkoxy sulfone | β-acyloxy sulfone

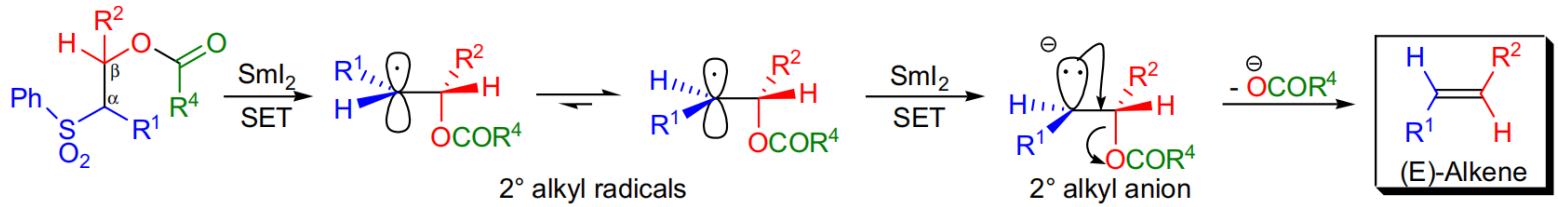
R^1 = H, alkyl, aryl; R^2, R^3 = H, alkyl, aryl, alkenyl; R^4 = alkyl, aryl; X = Cl, Br, OCOR

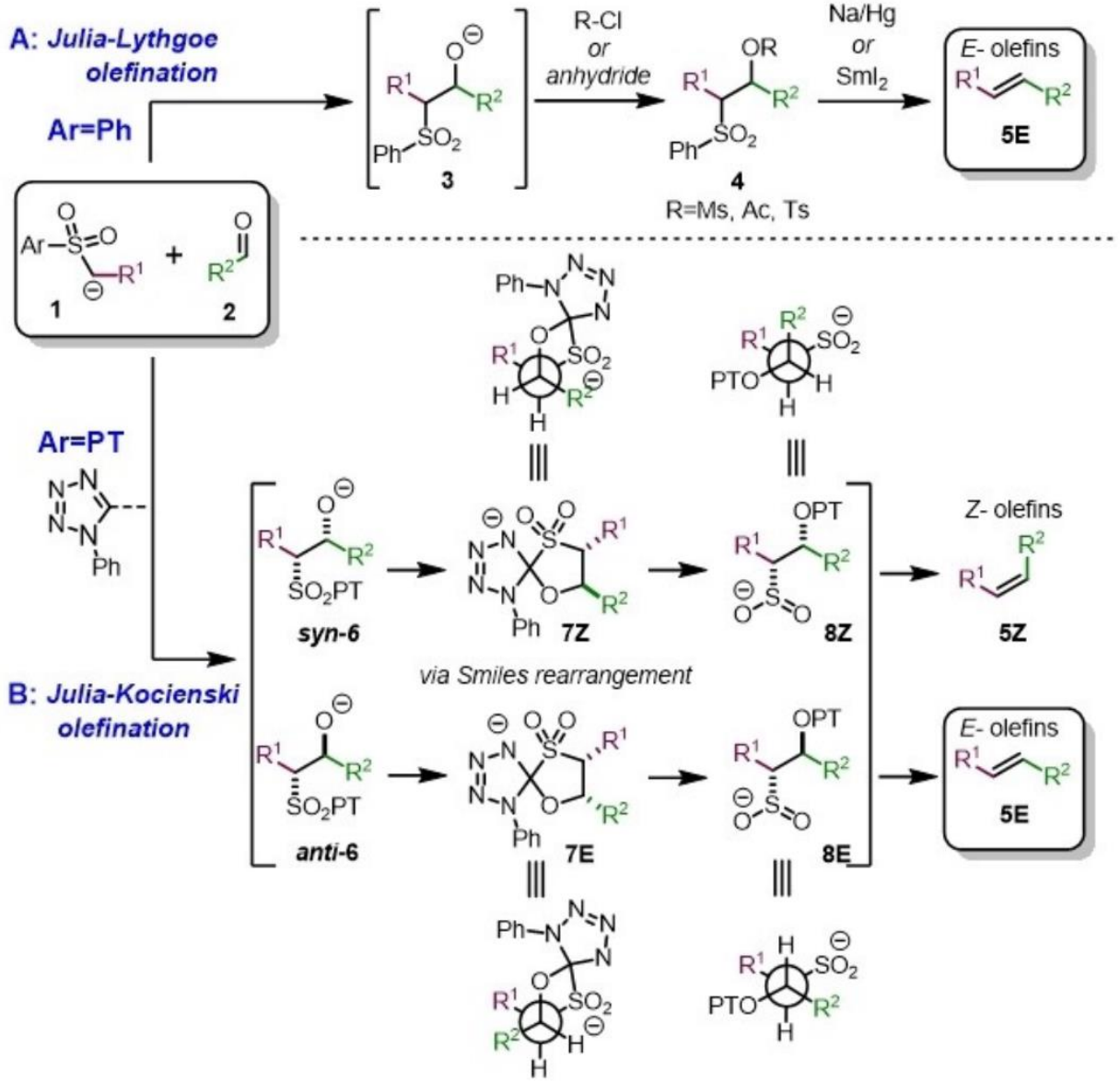
Modified (One-pot) Julia olefination:



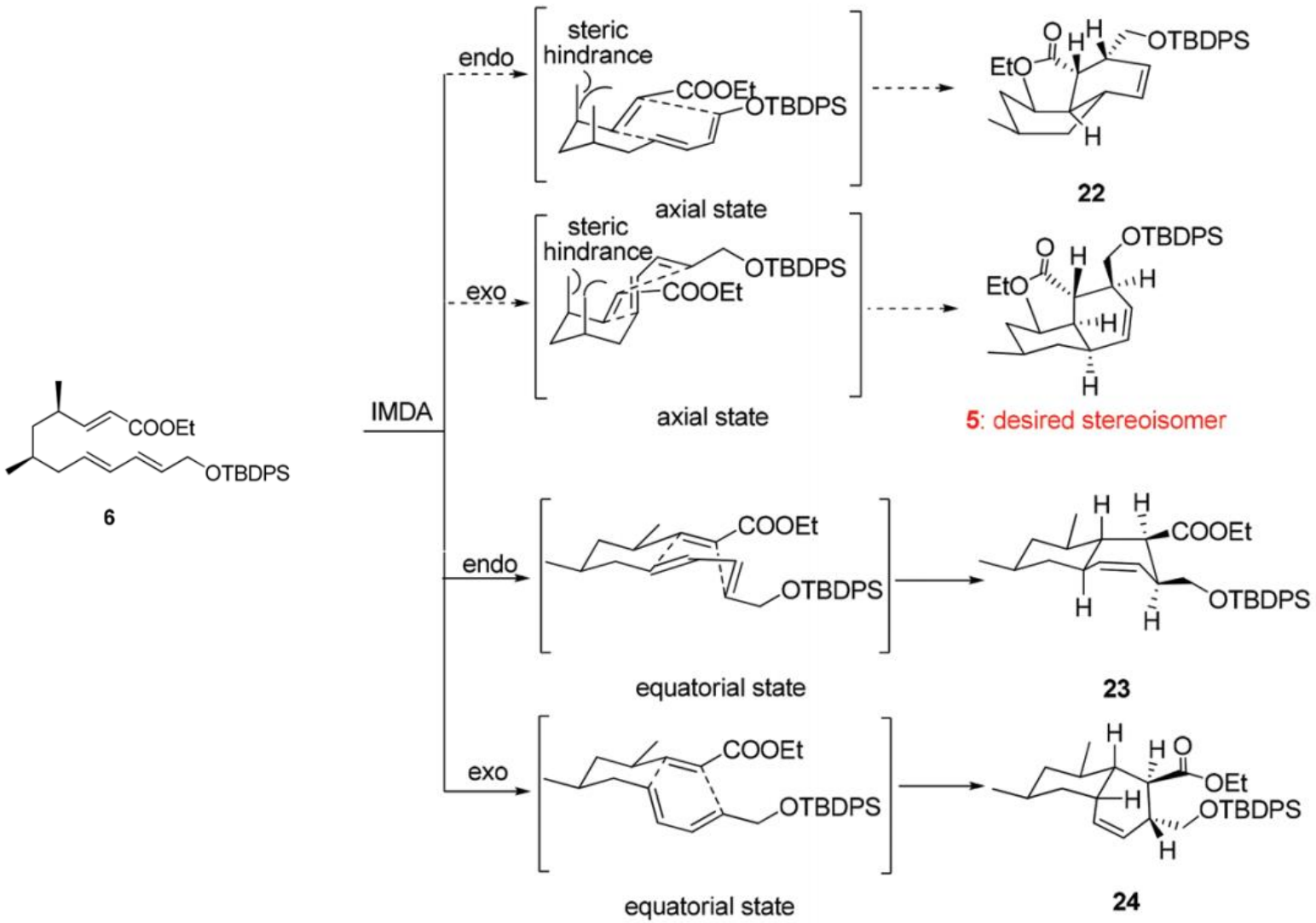
Het = benzothiazol-2-yl (BT) | β-alkoxysulfone | metal salt of benzothiazol-2-ol





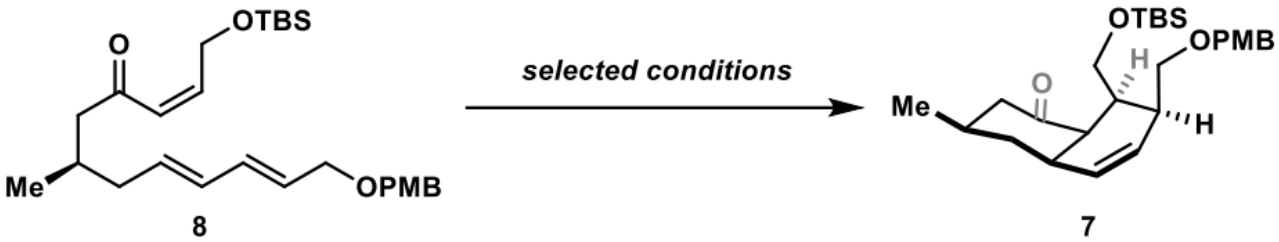


Eur. J. Org. Chem., **2023**, *26*, e2022017.

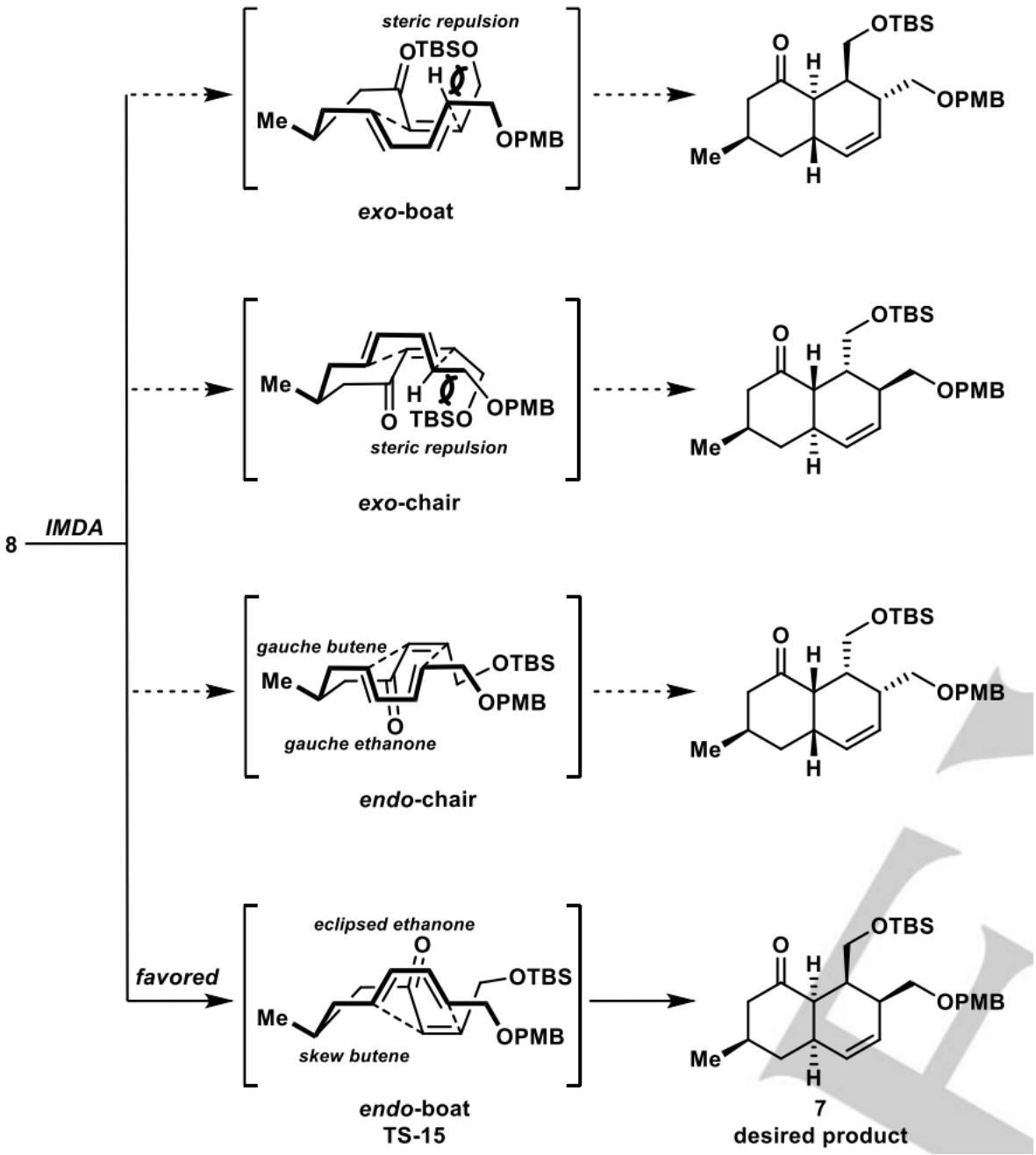


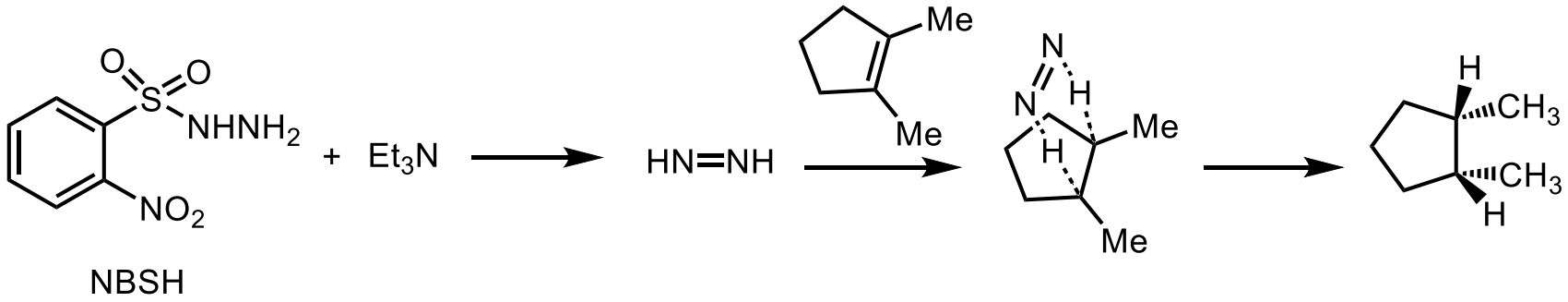
Org. Chem. Front., **2016**, *3*, 251.

Table S1. Condition screening of IMDA reaction



Entry	Condition	Solvent	Temp.	Isolated yield of 7
1	neat	---	rt.	< 10%
2	silica gel	DCM	rt.	< 10%
3	---	PhCl	160 °C	20%
4	Me_2AlCl (0.5 eq.)	DCM	0 °C	52%
5	$BF_3{\cdot}OEt_2$ (0.5 eq.)	DCM	-78 °C to -30 °C	24%
6	$EtAlCl_2$ (0.5 eq.)	DCM	0 °C	41%
7	$SnCl_4$ (0.5 eq.)	DCM	-78 °C to -30 °C	26%

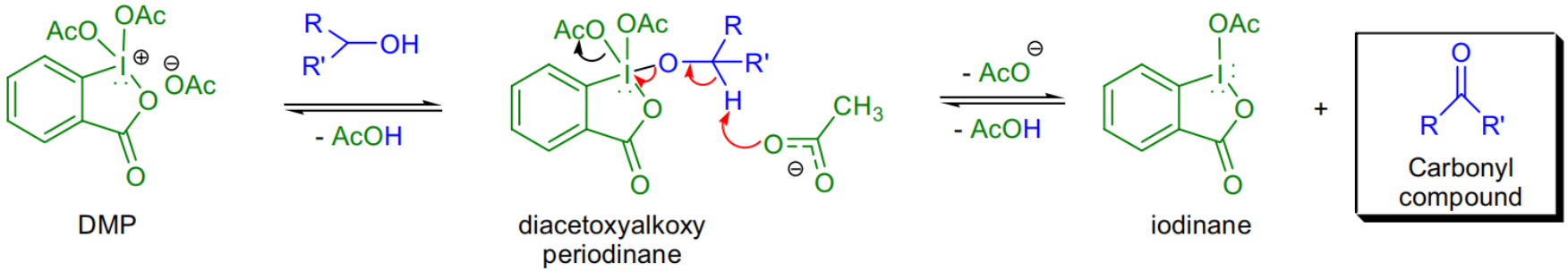

steric repulsion
OTBSO
H
Me
OPMB
exo-boat
OTBS
O
H
OPMB
Me
H
Me
H
O
TBSO
OPMB
steric repulsion
exo-chair
gauche butene
Me
OTBS
OPMB
O
gauche ethanone
endo-chair
8
IMDA
favored
eclipsed ethanone
O
OTBS
Me
OPMB
skew butene
endo-boat
TS-15
7
desired product



NBSH

DESS-MARTIN OXIDATION

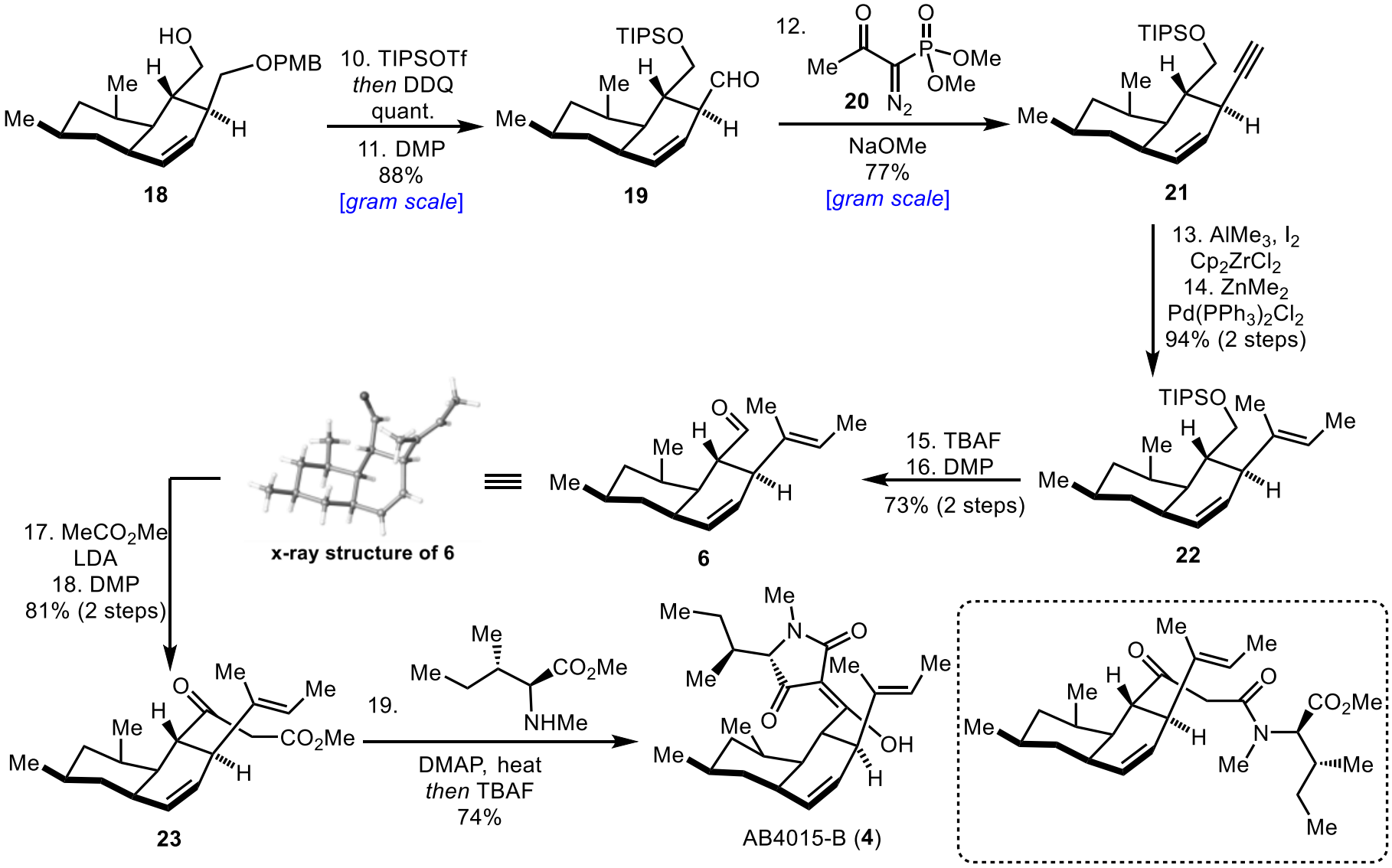
(References are on page 574)



DMP

diacetoxyalkoxy periodinane

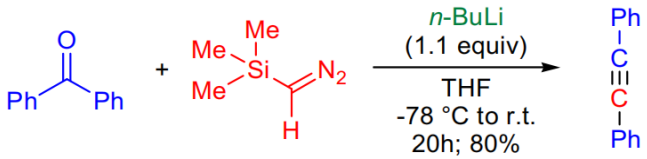
iodinane


HO
OPMB
Me
H
Me
H
18
10. TIPSOTf
then DDQ
quant.
11. DMP
88%
[gram scale]
TIPSO
CHO
Me
H
Me
H
19
12.
O
O
P
OMe
OMe
Me
20
N2
NaOMe
77%
[gram scale]
TIPSO
H
Me
Me
H
21
13. AlMe3, I2
Cp2ZrCl2
14. ZnMe2
Pd(PPh3)2Cl2
94% (2 steps)
TIPSO
Me
H
Me
Me
Me
H
22
15. TBAF
16. DMP
73% (2 steps)
O
Me
H
Me
Me
Me
H
6
x-ray structure of 6
17. MeCO2Me
LDA
18. DMP
81% (2 steps)
O
Me
H
Me
Me
CO2Me
Me
H
23
19.
Me
Me
CO2Me
NHMe
DMAP, heat
then TBAF
74%
Me
N
O
Me
Me
Me
Me
O
Me
OH
H
AB4015-B (4)
Me
O
Me
Me
H
Me
O
CO2Me
Me
N
Me
Me
Me

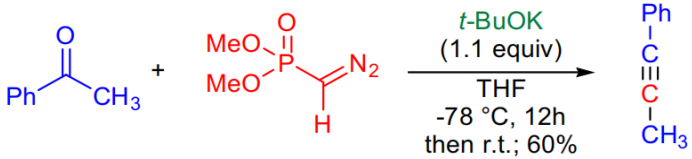
SEYFERTH-GILBERT HOMOLOGATION

(References are on page 672)

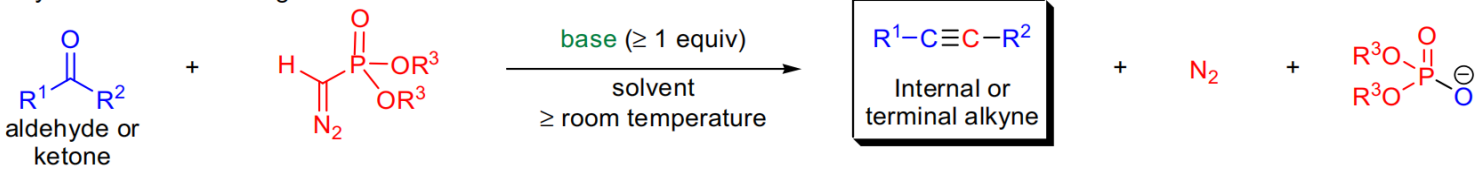
Colvin & Hamill (1973):



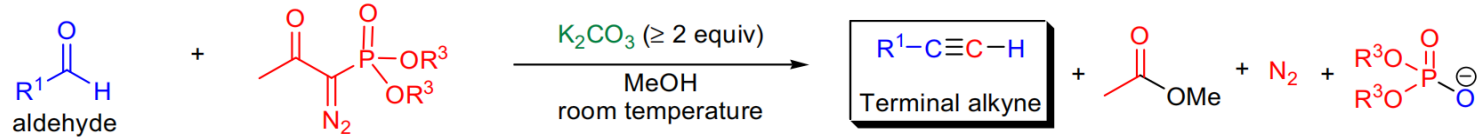
Gilbert & Weerasooriya (1979):



Seyferth-Gilbert homologation:

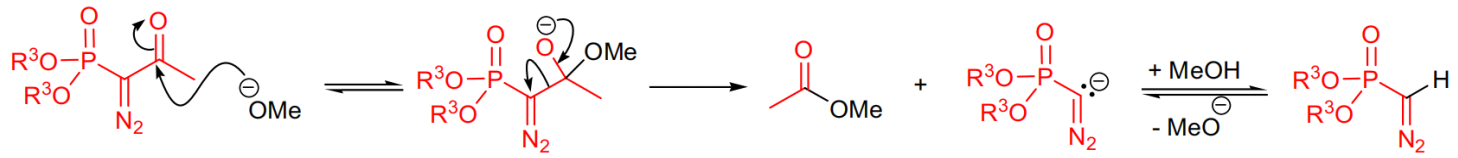


Modification for the synthesis of terminal alkynes (Ohira & Bestmann):

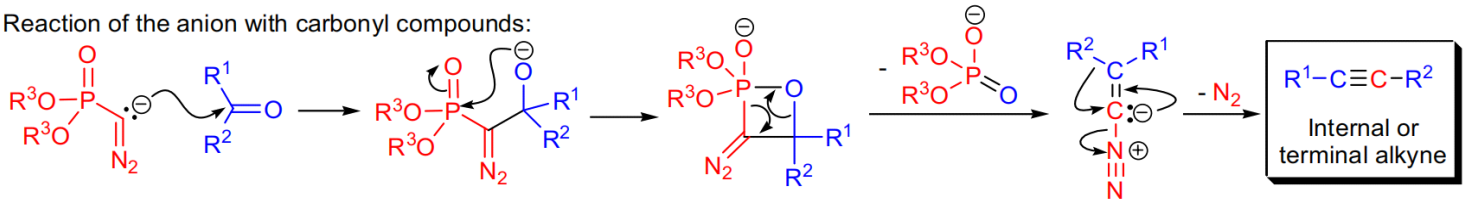


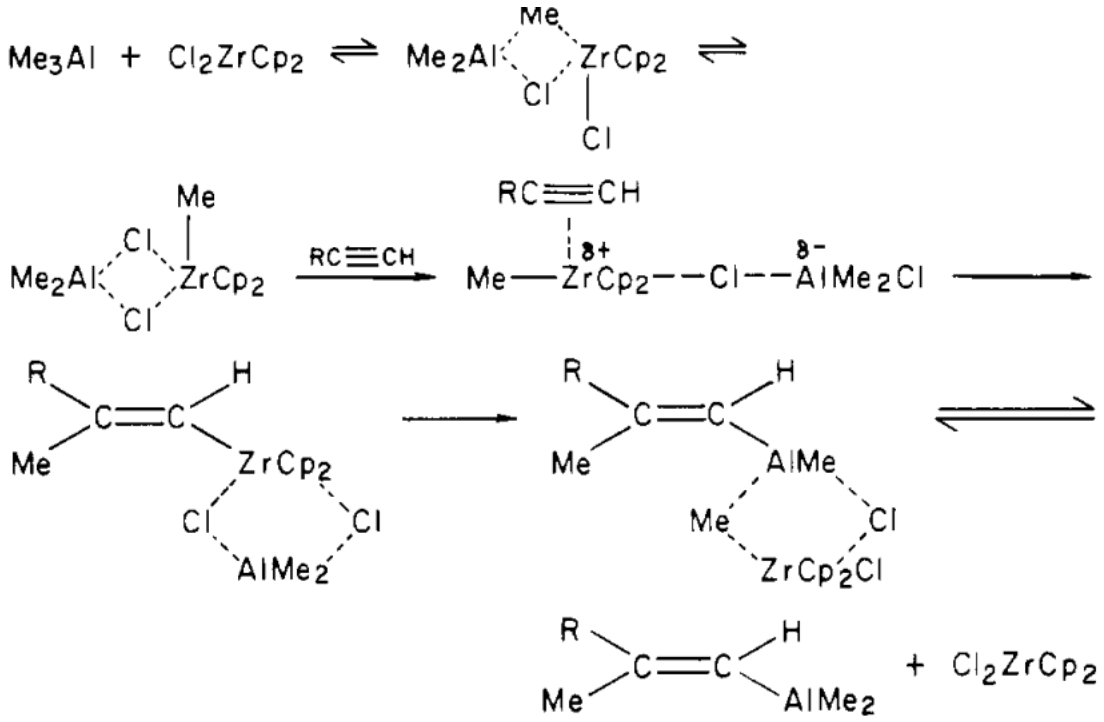
R^1 = alkyl, aryl, heteroaryl; R^2 = H, aryl, heteroaryl; R^3 = Me, Et; base: *n*-BuLi, KO-*t*Bu

Formation of the dialkylphosphonodiazomethane from dialkyl-1-diazo-2-oxopropylphosphonate:

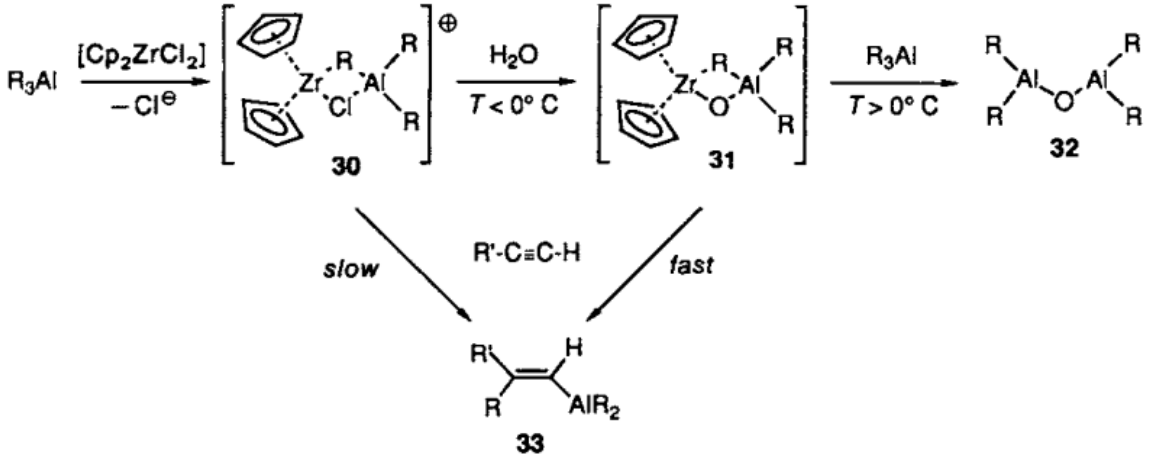


Reaction of the anion with carbonyl compounds:





J. Am. Chem. soc., **1985**, *107*, 6639.



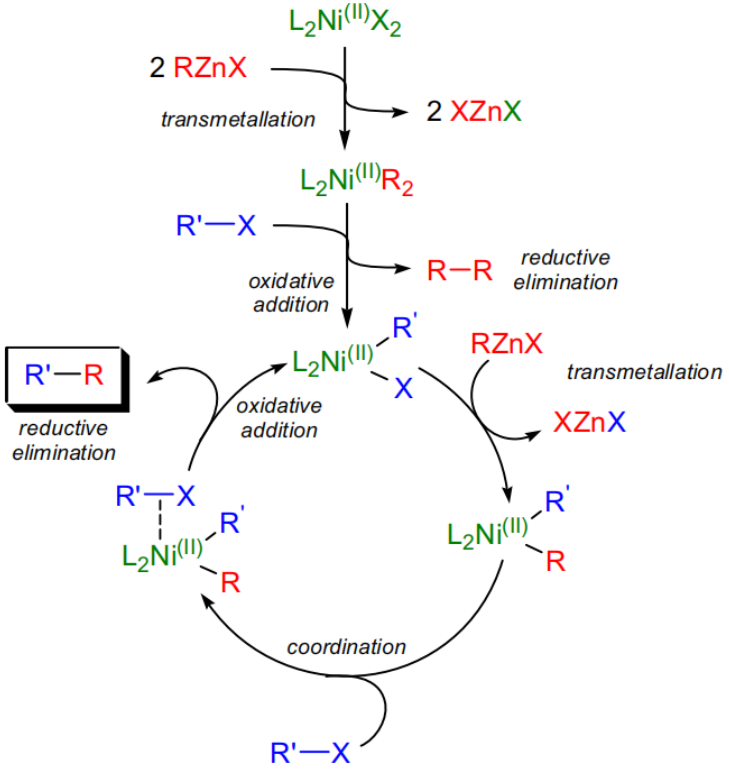
Angew. Chem. Int. Ed., **1993**, *32*, 1068.

NEGISHI CROSS-COUPLING

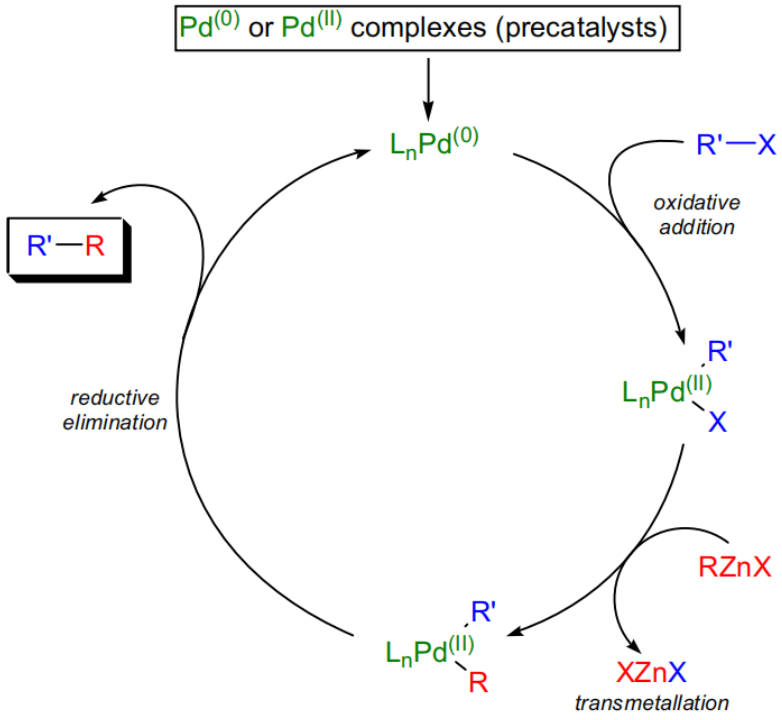
(References are on page 637)

Mechanism: [10]

Ni-catalyzed process:



Pd-catalyzed process:



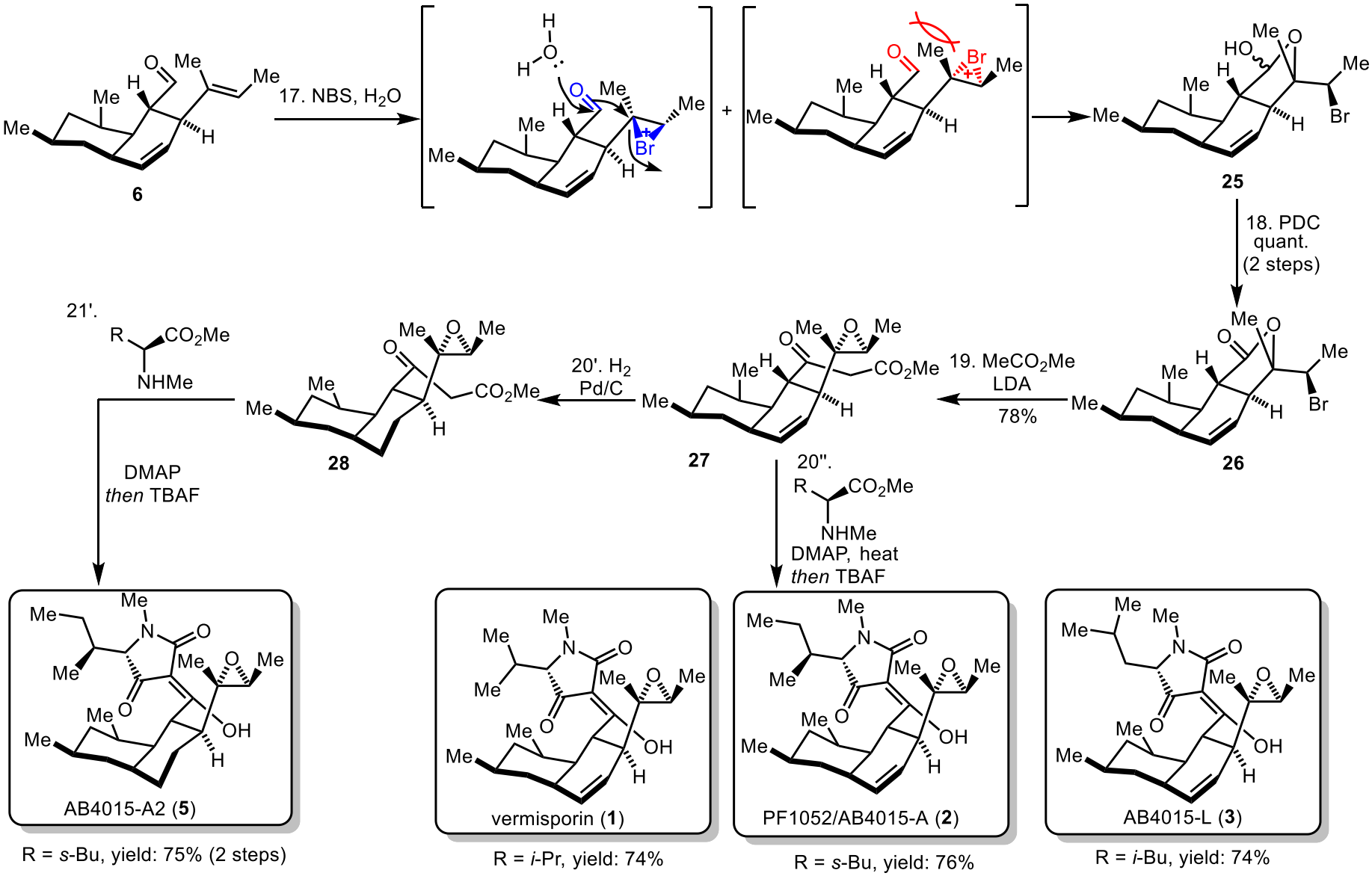
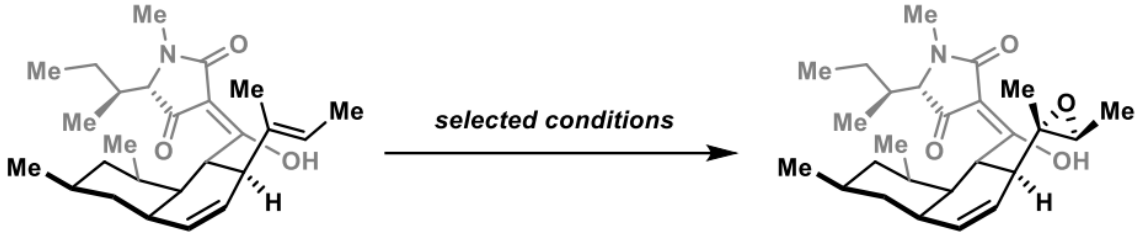

6
17. NBS, H_2O
25
18. PDC
quant.
(2 steps)
26
19. $MeCO_2Me$
LDA
78%
27
20'. H_2
Pd/C
28
21'.
DMAP
then TBAF
20''.
DMAP, heat
then TBAF
AB4015-A2 (**5**)
R = *s*-Bu, yield: 75% (2 steps)
vermisporin (**1**)
R = *i*-Pr, yield: 74%
PF1052/AB4015-A (**2**)
R = *s*-Bu, yield: 76%
AB4015-L (**3**)
R = *i*-Bu, yield: 74%

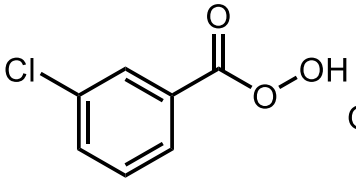
Table S2. Attempted epoxidation of AB4015-B (**4**) to obtain PF1052/AB4015-A (**2**)



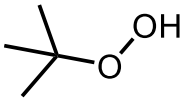
AB4015-B
4

PF1052
AB4015-A
2

Entry	Condition	Solvent	Temp.	Result
1	*m*-CPBA	DCM	0 °C	no desired product
2	*m*-CPBA, $NaHCO_3$	DCM	0 °C	no desired product
3	TBHP, $VO(acac)_2$	DCM	0 °C to rt.	decomposition
4	TBHP, $Ti(O^iPr)_4$	DCM	0 °C to rt.	decomposition
5	DMDO	acetone	-78 °C to 0 °C	decomposition
6	Oxone®, $NaHCO_3$	acetone/H_2O	0 °C to rt.	complex mixture
7	Oxone®, $NaHCO_3$ 18-crown-6	MeCN/ H_2O	0 °C to rt.	complex mixture
8[1]	(−)-Shi's ketone Shi's epoxidation	DMM/MeCN/H_2O	-10 °C	complex mixture
9[2]	(+)-Shi's ketone Shi's epoxidation	DMM/MeCN/H_2O	-10 °C	complex mixture

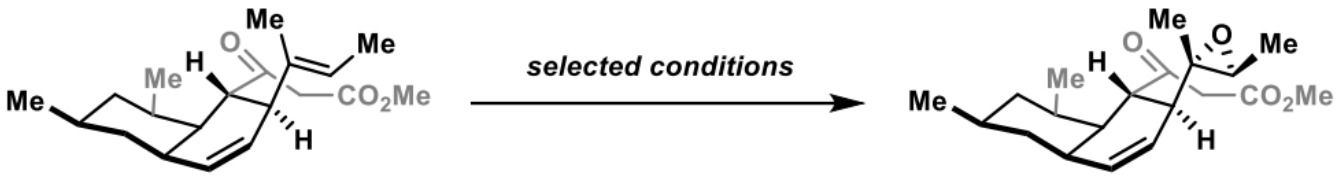
m-CPBA: 

Oxone:$KHSO_5$ DMDO: 

TBHP: 

DMM :二丙二醇二甲醚

Table S3. Attempted epoxidation of compound **23** to obtain compound **27**

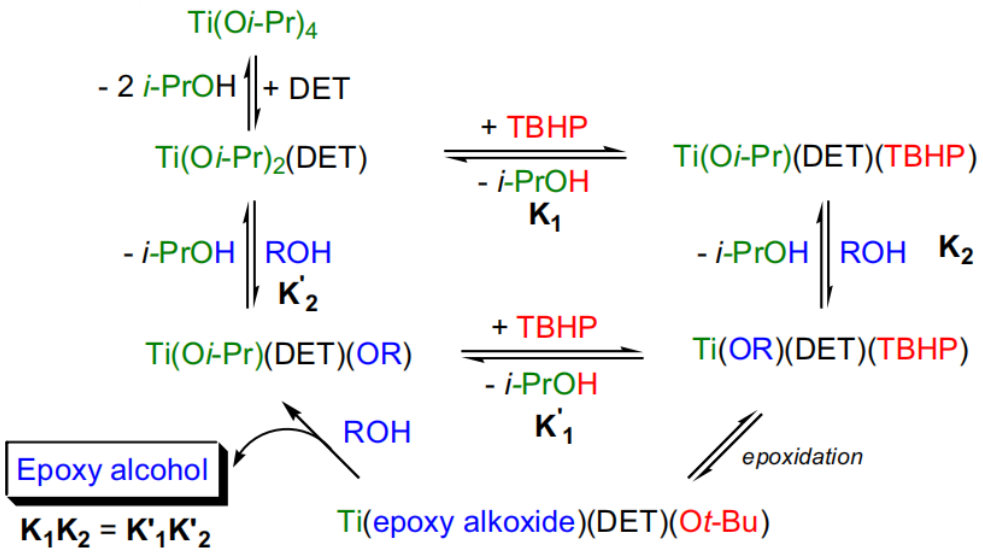


23 27

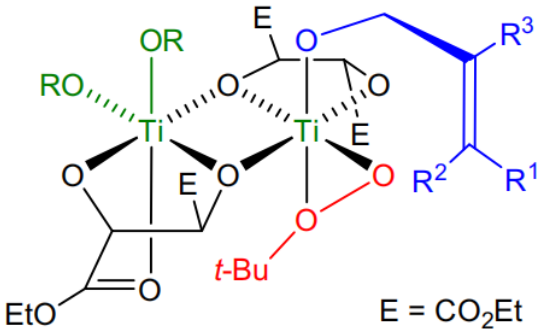
Entry	Condition	Solvent	Temp.	Result
1	*m*-CPBA	DCM	0 °C	no desired product
2	*m*-CPBA, $NaHCO_3$	DCM	0 °C	no desired product
3	TBHP, $VO(acac)_2$	DCM	0 °C to rt.	no reaction
4	DMDO	acetone	-78 °C to 0 °C	complex mixture
5	Oxone®, $NaHCO_3$	acetone/H_2O	0 °C to rt.	complex mixture

SHARPLESS ASYMMETRIC EPOXIDATION

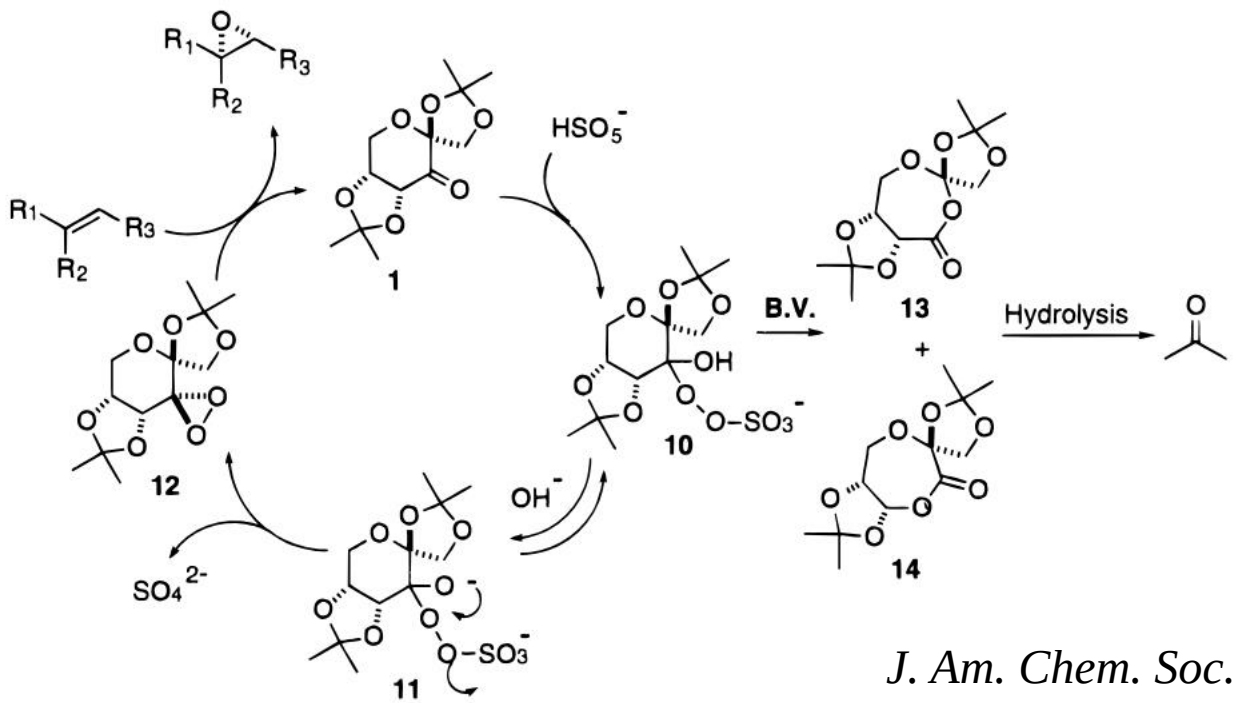
(References are on page 675)



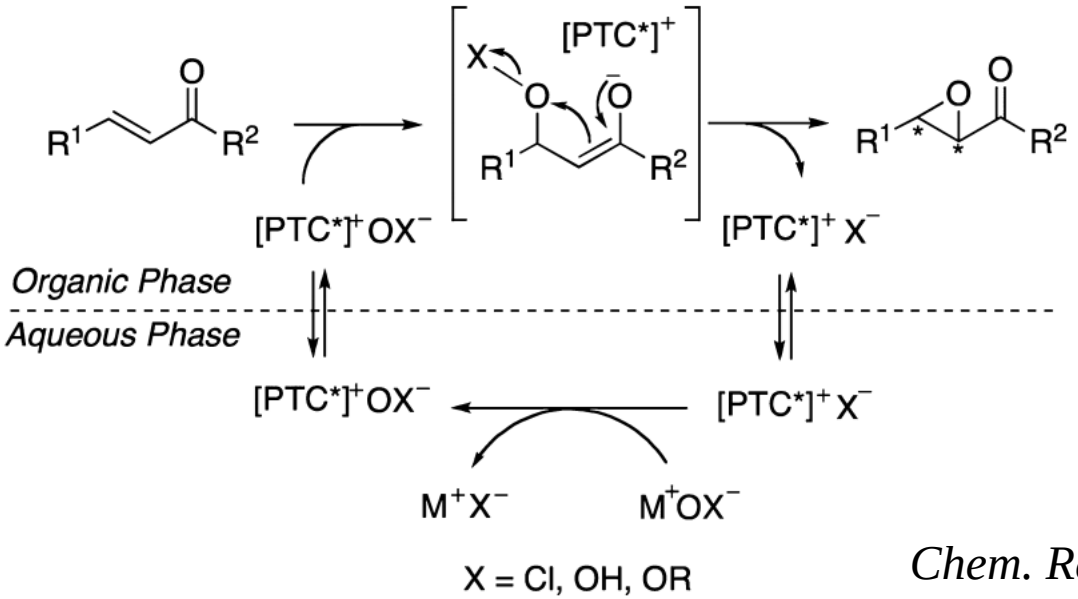
Transition state of epoxidation:



$$\text{Rate} = \frac{[\text{Ti}(\text{O}i\text{-Pr})_2(\text{DET})]\,[\text{TBHP}]\,[\text{ROH}]}{[i\text{-PrOH}]^2}$$



J. Am. Chem. Soc., **1996**, *118*, 9806.
J. Am. Chem. Soc., **1997**, *119*, *11224*.



Chem. Rev., **2014**, *114*, 8199.