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Communication

Total Synthesis of (−)-Daphnezomines A and B

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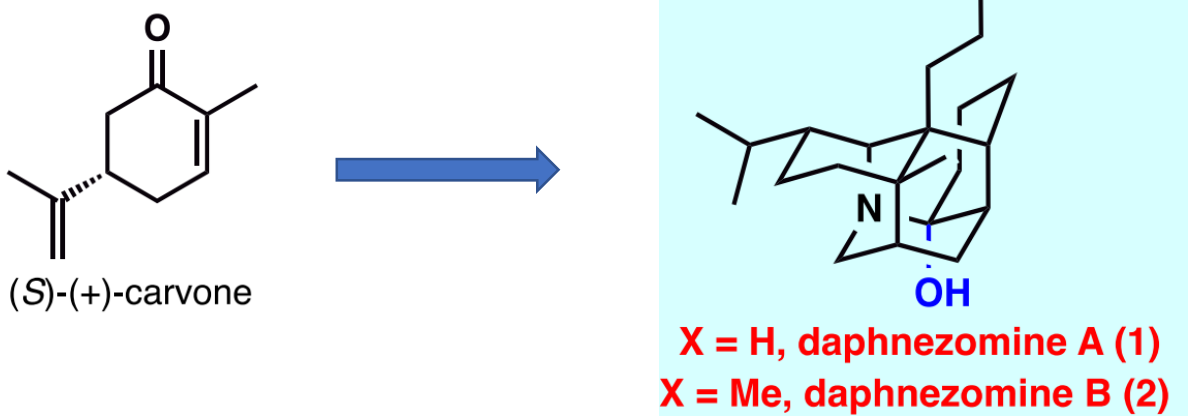


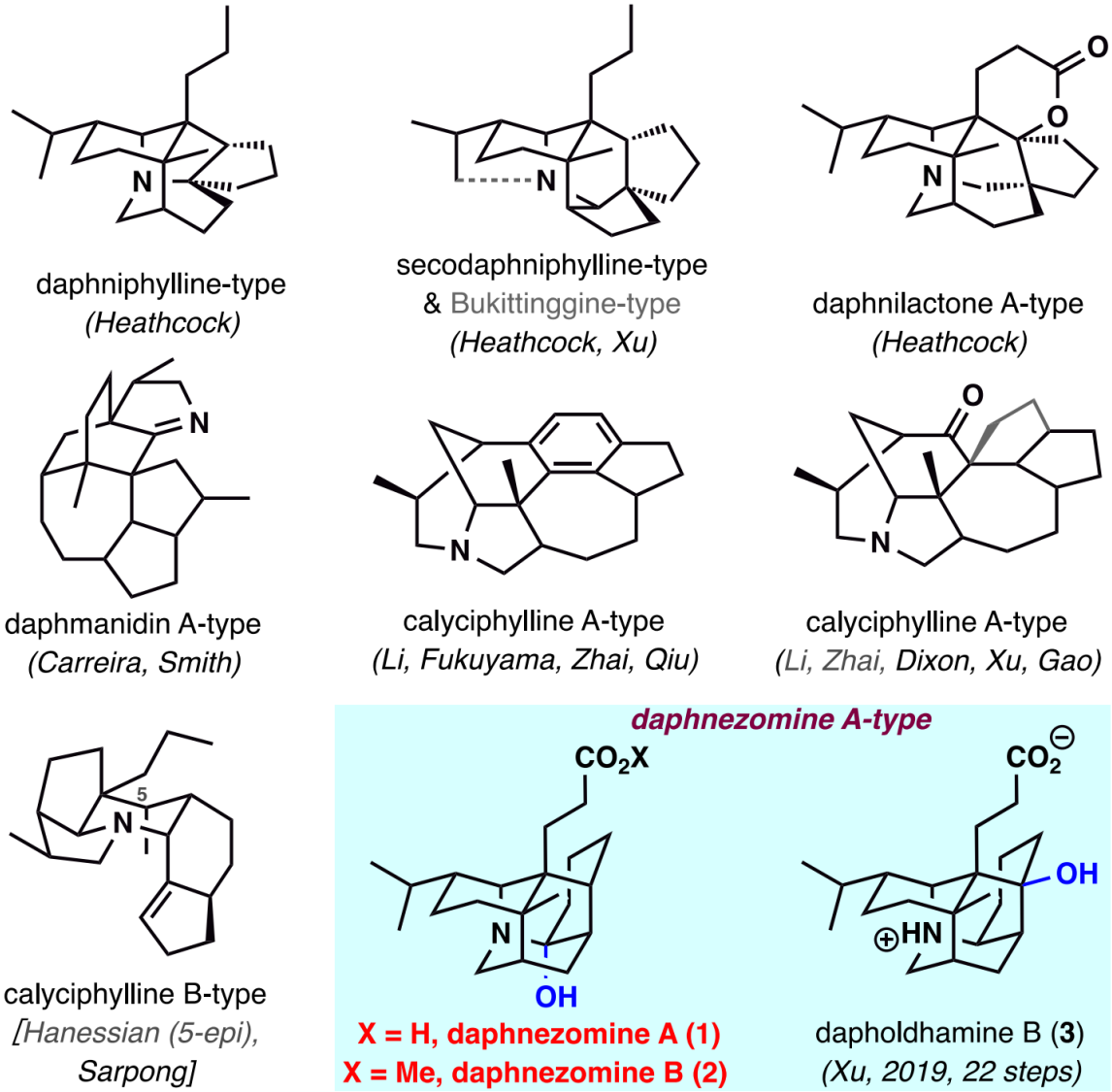
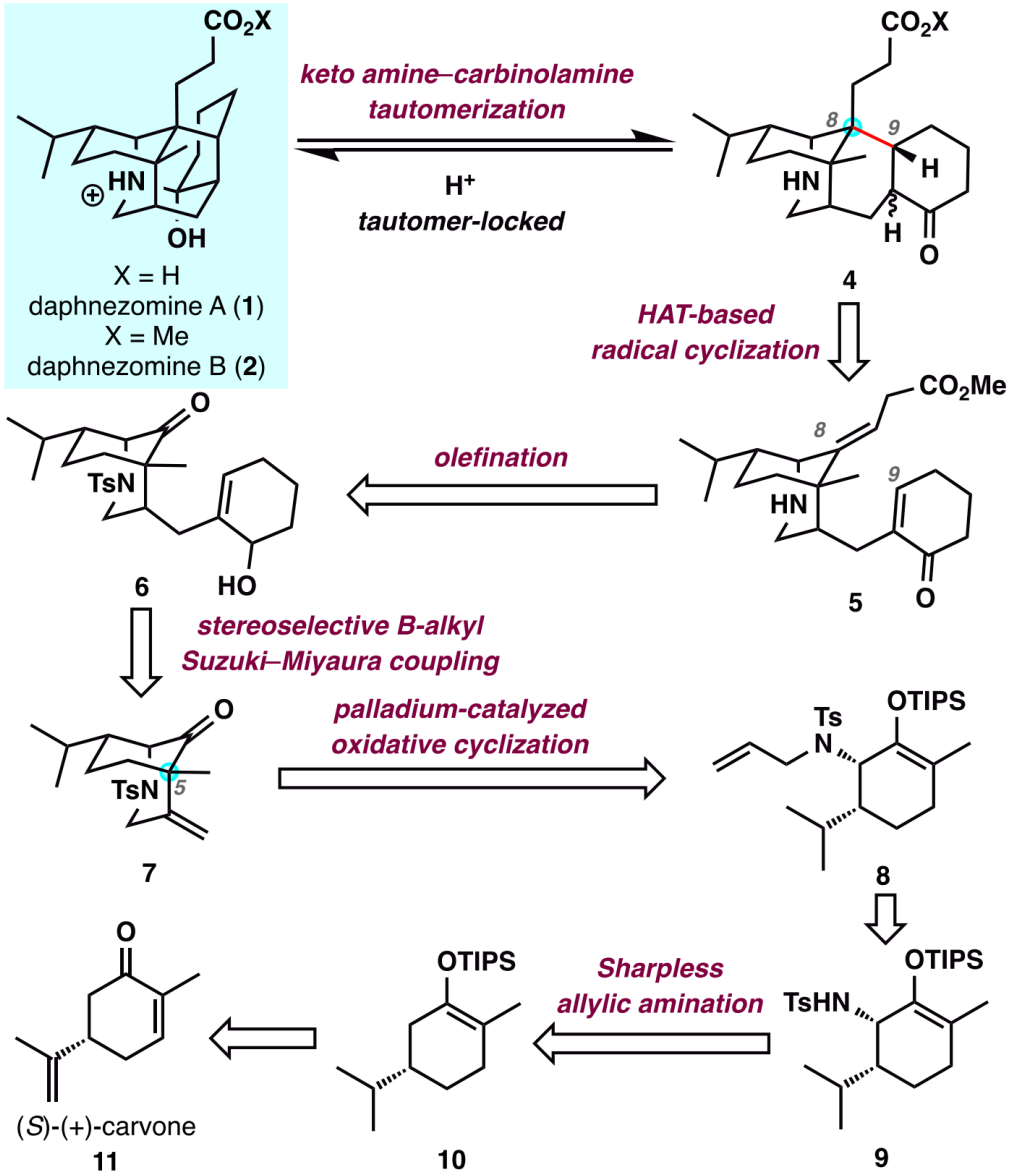
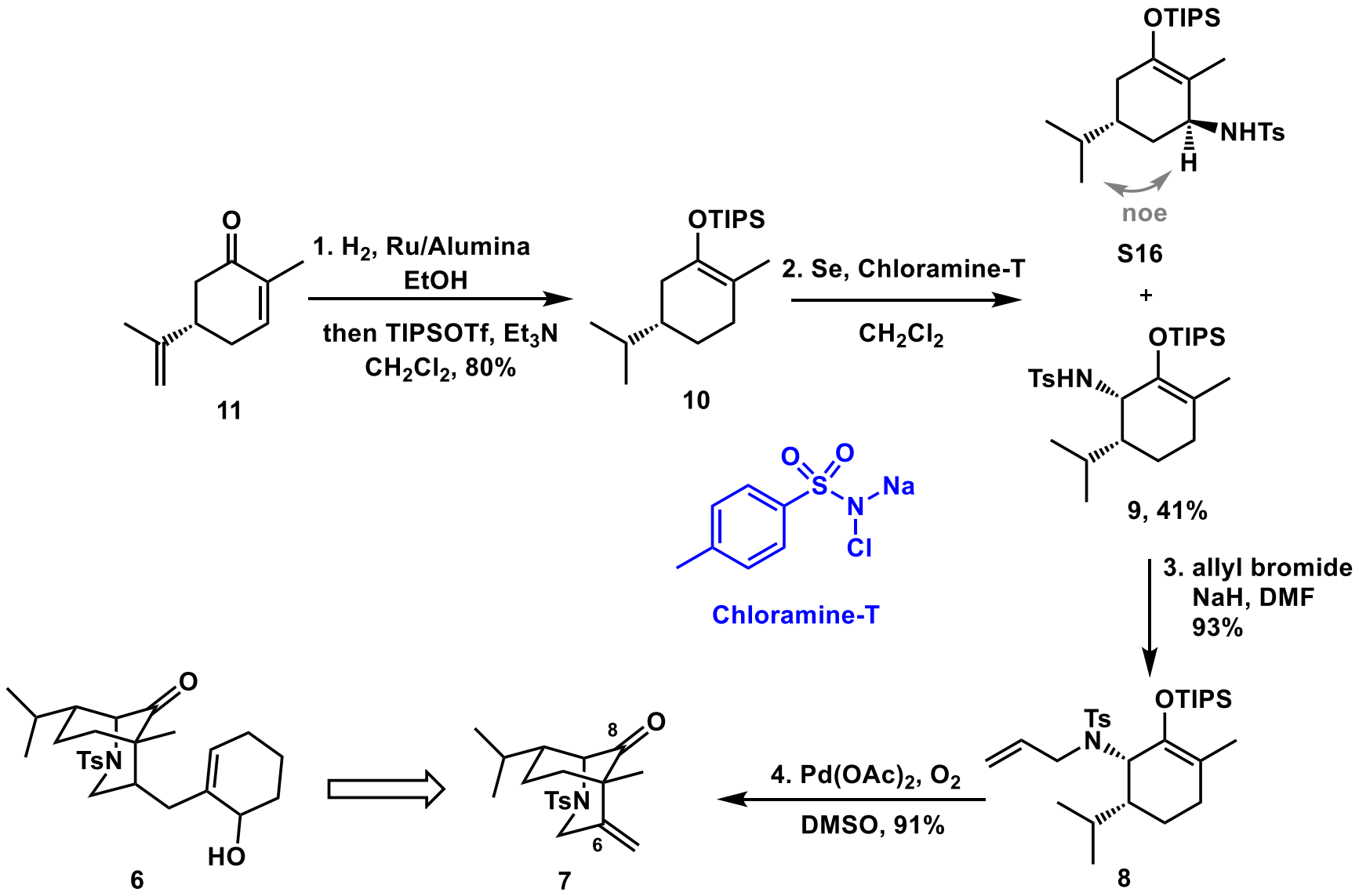


Figure 1. Frameworks of previously synthesized *Daphniphyllum* alkaloids, and the structures of daphnezomine A-type alkaloids.

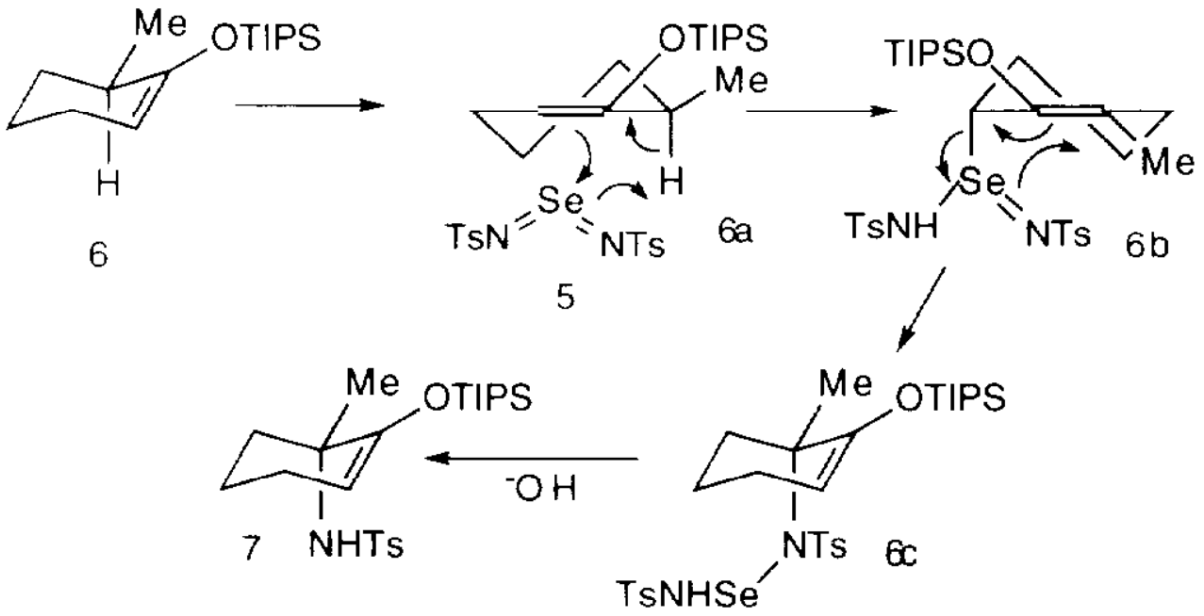
Scheme 1. Retrosynthetic Analysis




OTIPS
NHTs
H
noe
S16
+
OTIPS
TsHN
9, 41%
O
1. H2, Ru/Alumina
EtOH
then TIPSOTf, Et3N
CH2Cl2, 80%
11
OTIPS
10
2. Se, Chloramine-T
CH2Cl2
O
O
S
N
Na
Cl
Chloramine-T
3. allyl bromide
NaH, DMF
93%
OTIPS
Ts
N
8
4. Pd(OAc)2, O2
DMSO, 91%
O
TsN
HO
6
8
O
TsN
6
7

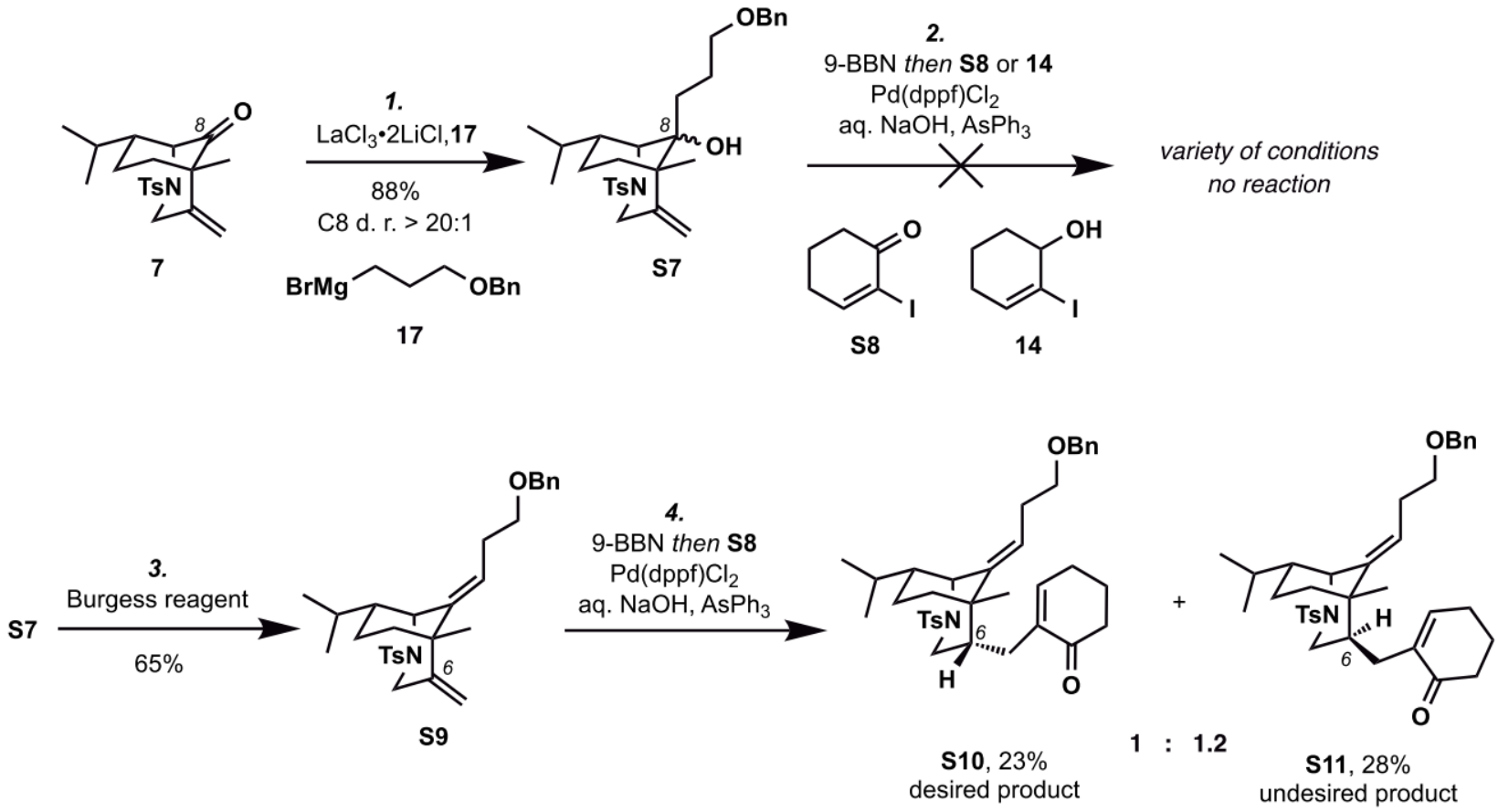
Sharpless allylic amination

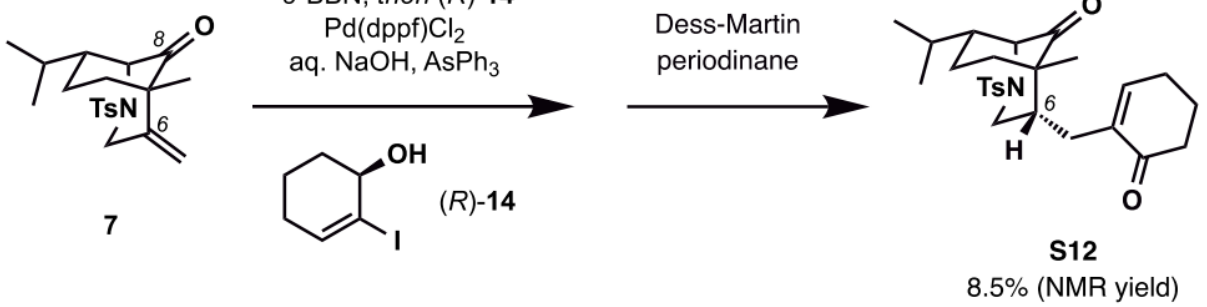
Scheme 3

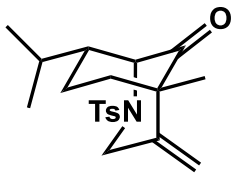


Tetrahedron, **1995**, *51*, 11087

Scheme S3. Attempts to a Protecting Group Free *B*-Alkyl Suzuki-Miyaura Reaction

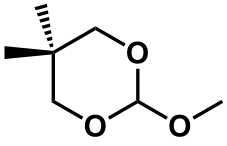






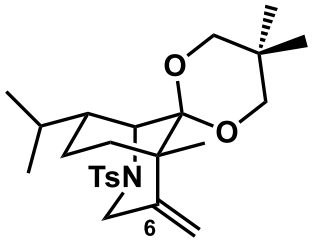
7

5.



12

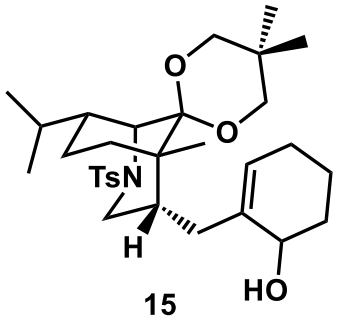
neopentylglycol
p-TsOH, THF, 80%



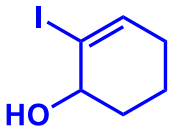
13

6. 9-BBN
then 14, $Pd(dppf)Cl_2$
aq. NaOH, $AsPh_3$

THF, C6 d. r. > 20:1



15

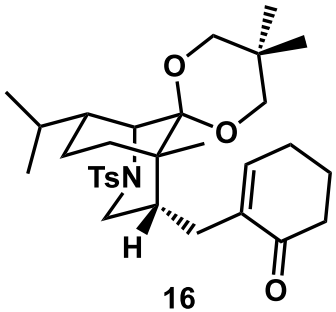


(*R*)-14, 94% ee
or *rac*-14

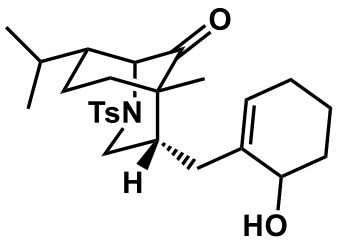
DMP
81%

7. TFA,
then aq. NaOH
C11 d. r. = 1:1

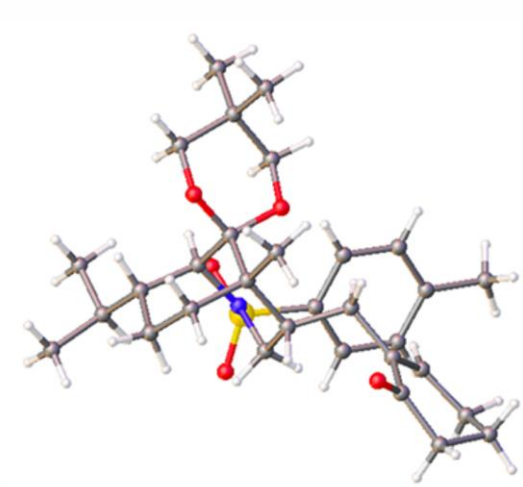
61% over 2 steps
using (*R*)-14;
58% over 2 steps
using *rac*-14



16

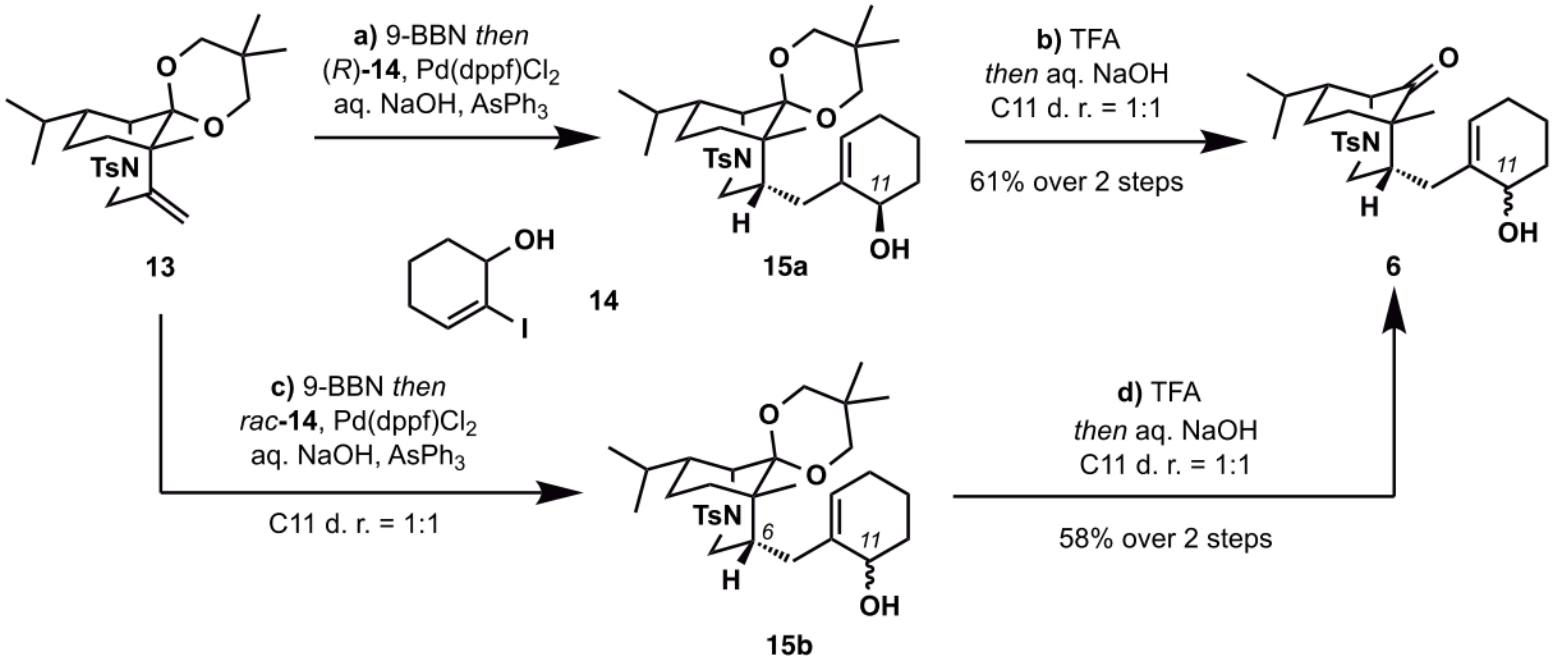


6



X-ray of **16**

Scheme S2. Examination of C11 Allylic Alcohol Epimerization in the Deprotection Process



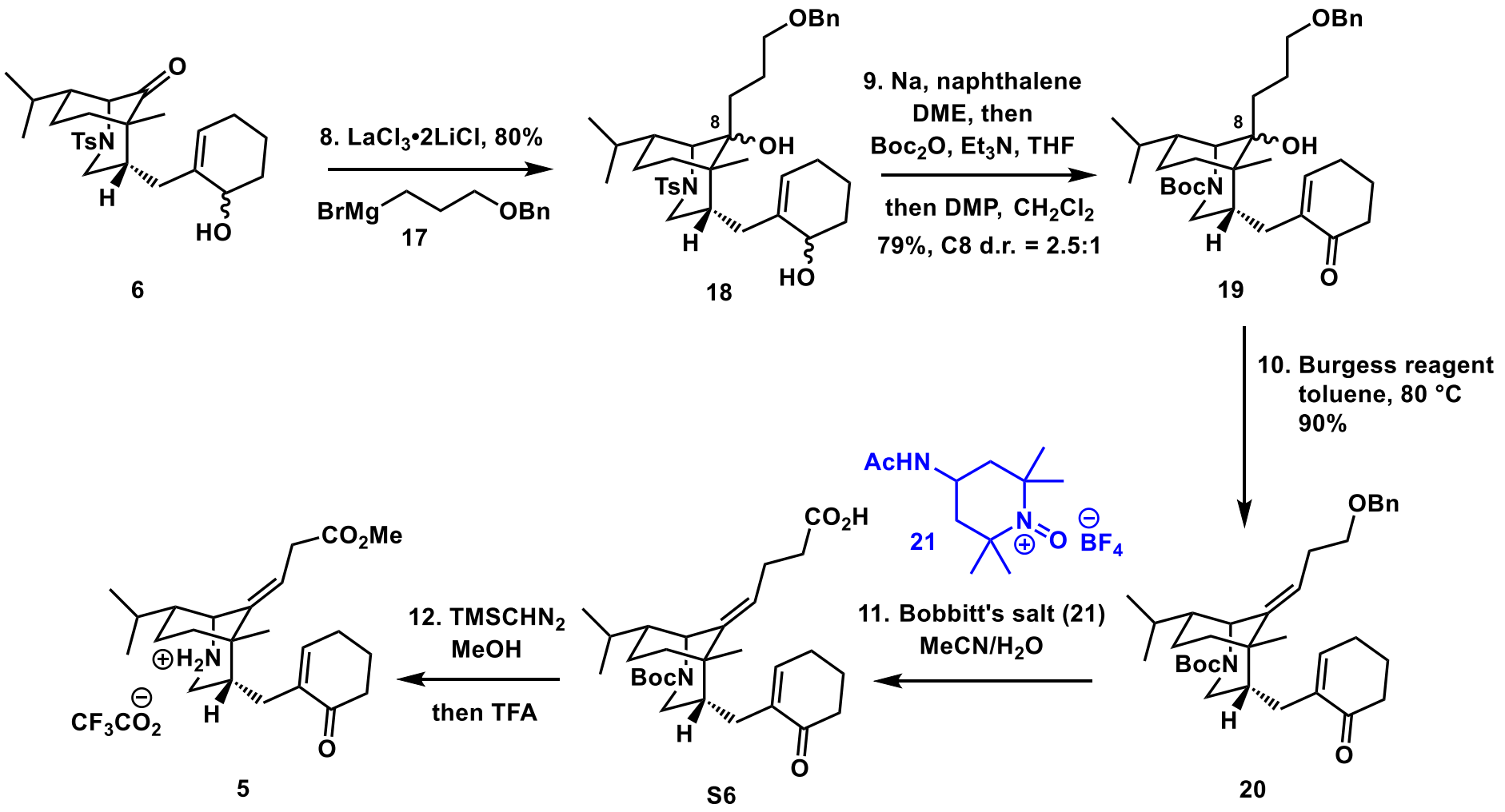
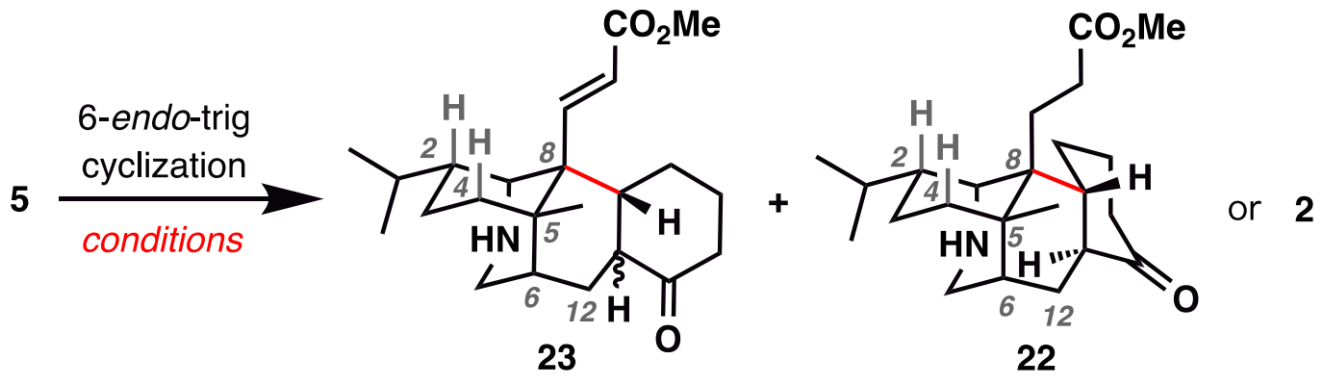
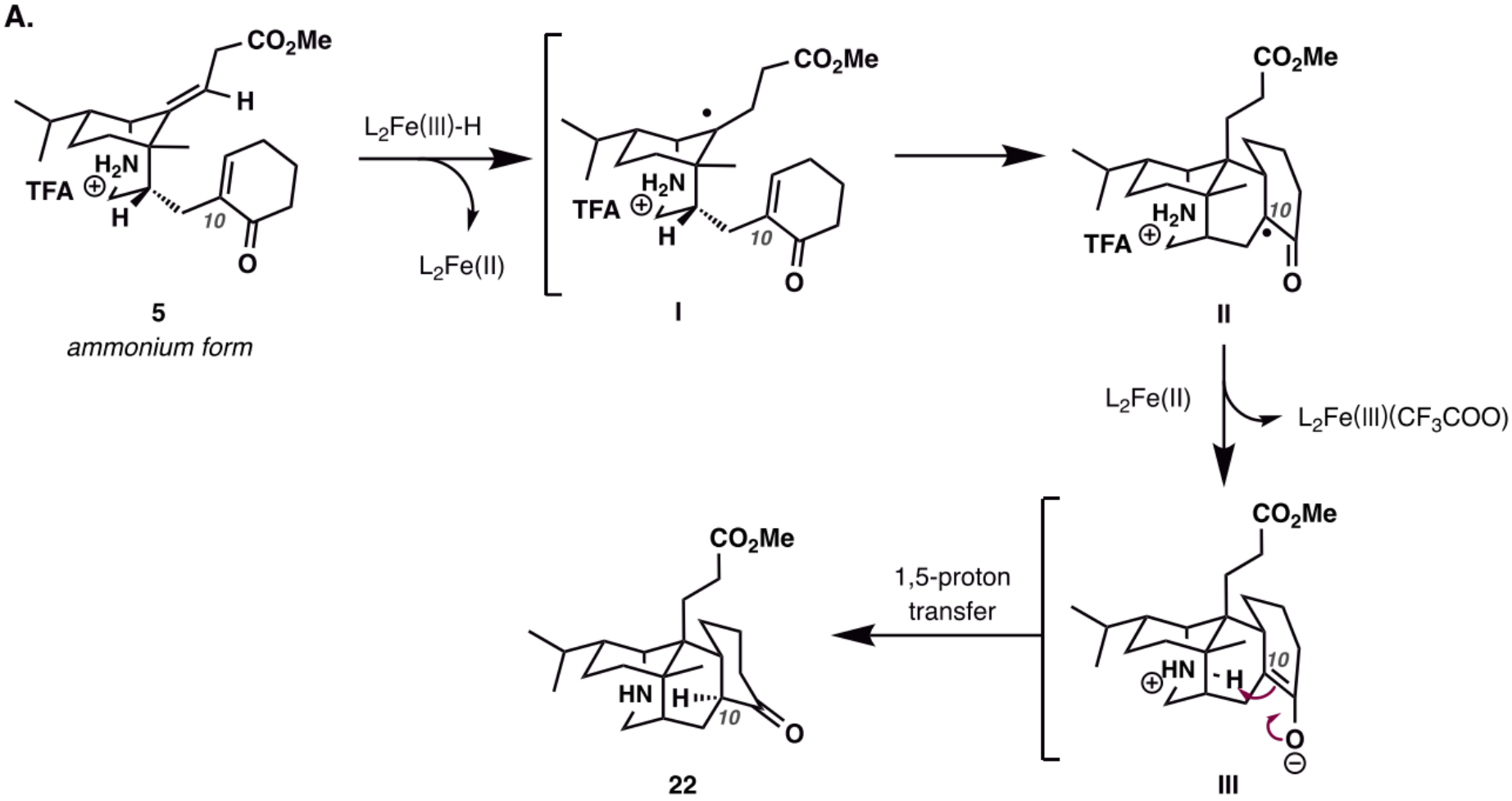

6
8. LaCl3•2LiCl, 80%
BrMg
OBn
17
18
9. Na, naphthalene
DME, then
Boc2O, Et3N, THF
then DMP, CH2Cl2
79%, C8 d.r. = 2.5:1
19
10. Burgess reagent
toluene, 80 °C
90%
20
AcHN
21
BF4
11. Bobbitt's salt (21)
MeCN/H2O
S6
12. TMSCHN2
MeOH
then TFA
5
CF3CO2

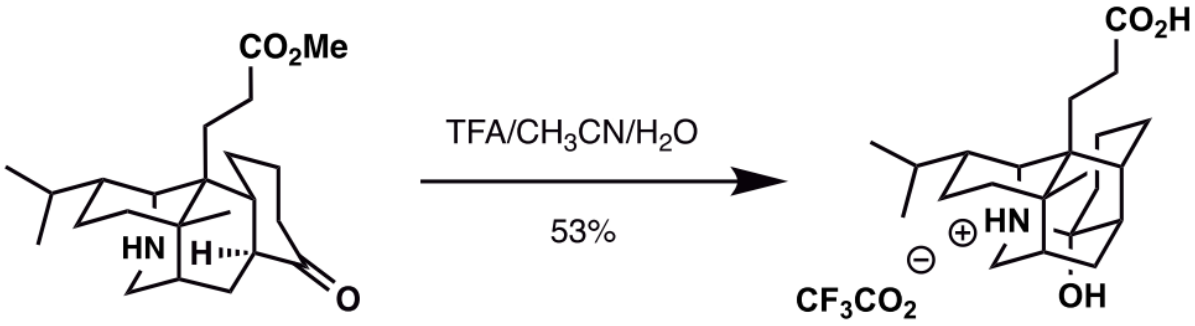
Table 1. Investigation of the 6-*endo*-trig Cyclization



Entry	Conditions[a]	23	22[b]	2
1	Lewis acids: BF_3•2AcOH, BF_3•Et_2O, $FeCl_3$, AgOTf, $AlCl_3$ *et al. (for details, see Table S1)*	0	-	-
2	bases: Et_3N, Pyridine, DBU, LDA, LiHMDS KHMDS *et al.* (*for details, see Table S2)*	0	-	-
3	$Fe(acac)_3$, $PhSiH_3$, EtOH, 60 °C	-	16%	ND
4	$Fe(acac)_3$, Ph(*i*-PrO)SiH_2, EtOH, 60 °C	-	17%	ND
5	$Fe(dibm)_3$, Ph(*i*-PrO)SiH_2, EtOH, 60 °C	-	5%	ND
6	$Fe(acac)_3$, Ph(*i*-PrO)SiH_2, EtOH/$(CH_2OH)_2$, 60 °C	-	22%	ND
7	$Fe(acac)_3$, Ph(*i*-PrO)SiH_2, THF/EtOH (0.02 M), 60 °C	-	26%	ND
8	**$Fe(acac)_3$, Ph(*i*-PrO)SiH_2, THF/EtOH (0.001 M), 60 °C**	-	31%(32%[c])	ND

[a]See SI for details. [b]Yield determined by ^1H NMR with CH_2Br_2 as an internal standard. [c]Isolated yield.


A.
CO2Me
H
H2N
TFA
H
10
O
5
ammonium form
L2Fe(III)-H
L2Fe(II)
I
II
L2Fe(II)
L2Fe(III)(CF3COO)
1,5-proton
transfer
HN
H
- H
III
22



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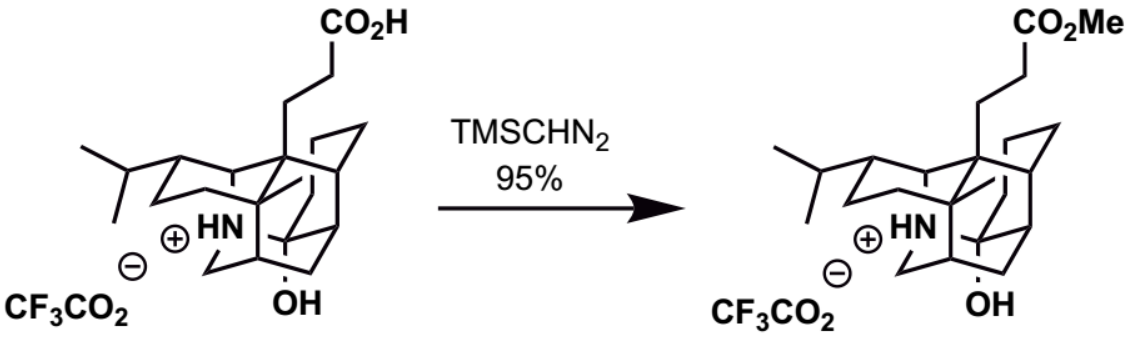
daphnezomine A•TFA
(**1**•TFA)



daphnezomine A•TFA
(**1**•TFA)

daphnezomine B•TFA
(**2**•TFA)