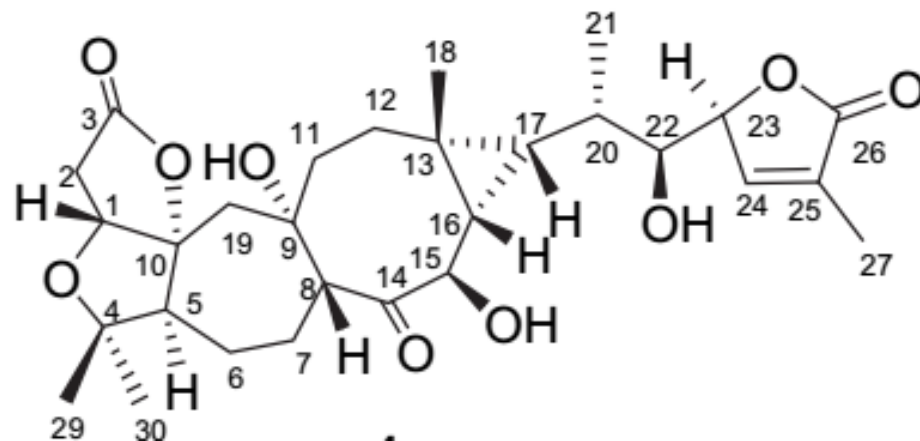


Asymmetric Total Synthesis of Pre-schisanartanin C

—Zhen Yang



1. Background

1.1 Introduction:

Chisandra: *S. chinensis* (*běi wǔ wèi zi*) and *S. sphenanthera* (*nan wǔ wèi zi*).

S. chinensis



S. sphenanthera

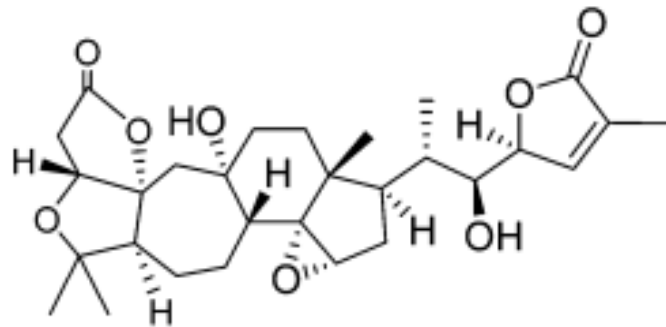


唐朝《新修本草》载“五味皮肉甘酸，核中辛苦，都有咸味”，具有收敛固涩、益气生津、补肾宁心等功效

1. Background

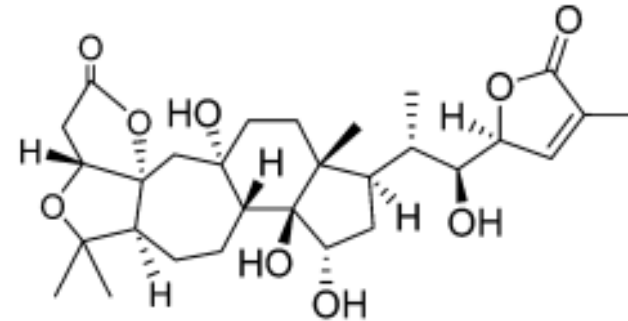
1.2 Triterpenoids from the Schisandraceae family :

1.2.1. Schiartane-type: micrandilactones B and C



micrandilactones B

weak anti-HIV-1 activity



micrandilactones C

anti-HIV-1 activity
 EC_{50} 7.71 $\mu\text{g}/\text{mL}$

Han-Dong Sun, *Nat. Prod. Rep.*, 2015, 32, 367

Han-Dong Sun, *Tetrahedron*, 2010, 66, 2306

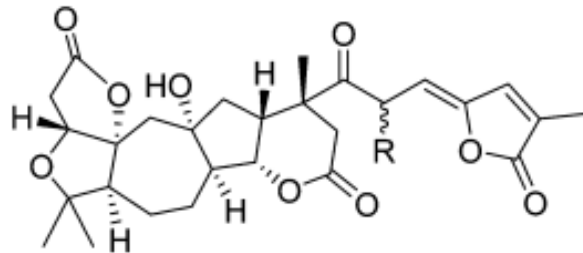
Han-Dong Sun, *Nat. Prod. Rep.*, 2008, 25, 871

1. Background

1.2 Triterpenoids from the Schisandraceae family :

1.2.2. Wuweiziartane-type

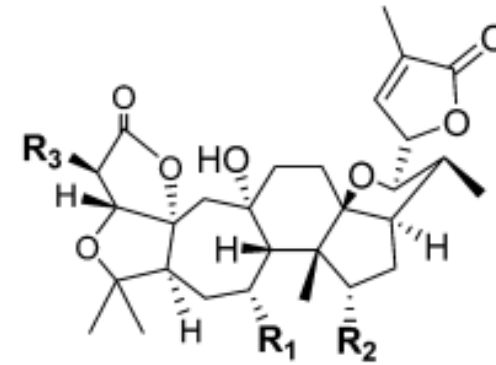
1.2.3. 18(13→14)-*abeo*-Schiartane-type



R = β -Me

R = α -Me

Wuweiziartane-type



R₁ = OAc, R₂ = OH, R₃ = H

R₁ = H, R₂ = OH, R₃ = H

R₁ = H, R₂ = OAc, R₃ = H

R₁ = H, R₂ = OAc, R₃ = OH

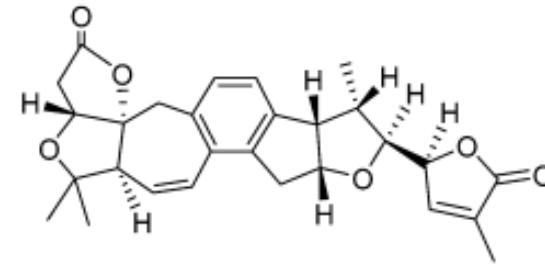
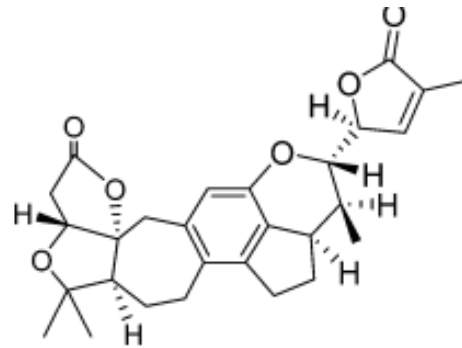
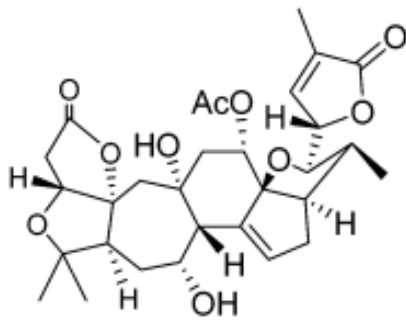
18(13→14)-*abeo*-Schiartane-type

all these compounds showed weak anti-HIV-1 activity

1. Background

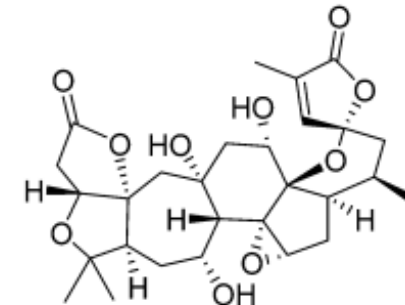
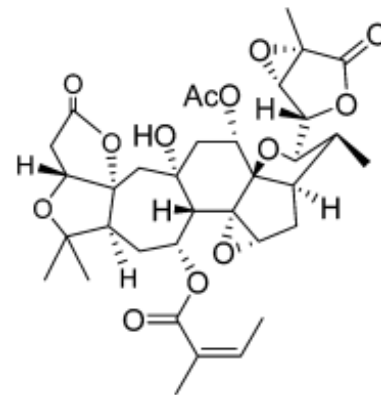
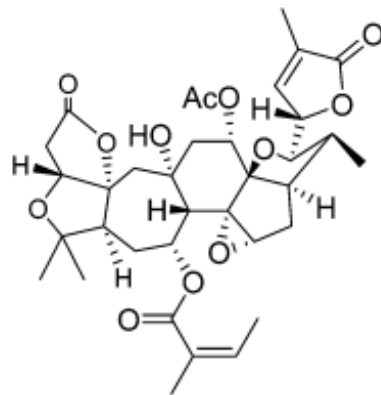
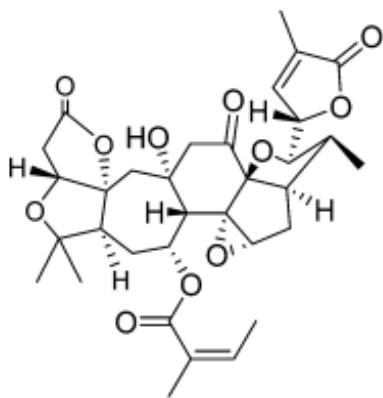
1.2 Triterpenoids from the Schisandraceae family :

1.2.4. 18-Norschiartane-type



Rubriflordilactone A
weak anti-HIV-1 activity

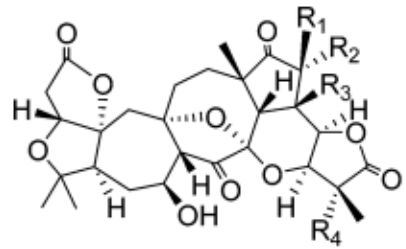
Rubriflordilactone B
 EC_{50} 9.75 μ g/ mL, against HIV-1 replication



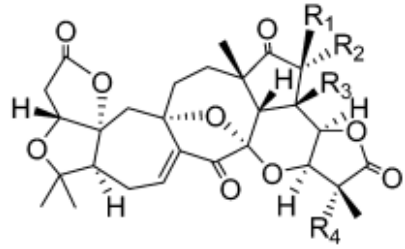
1. Background

1.2 Triterpenoids from the Schisandraceae family :

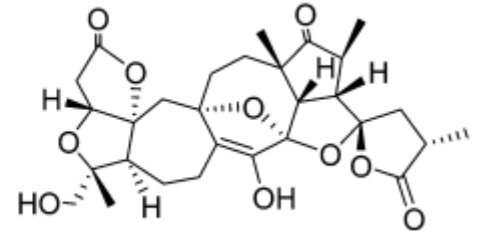
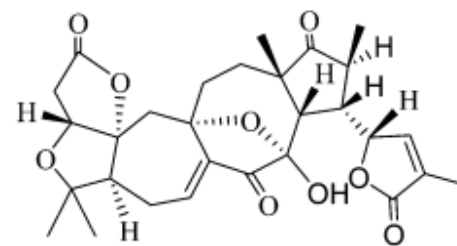
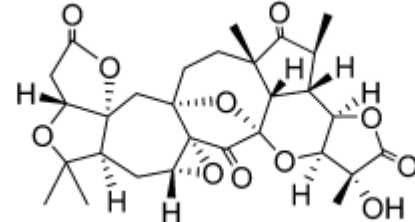
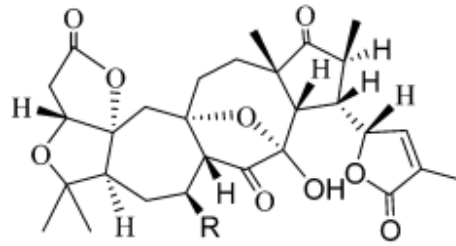
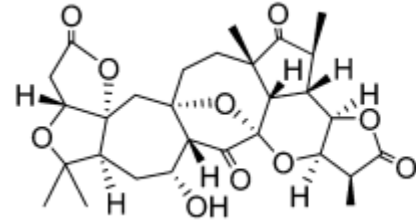
1.2.5. Schisanartane-type



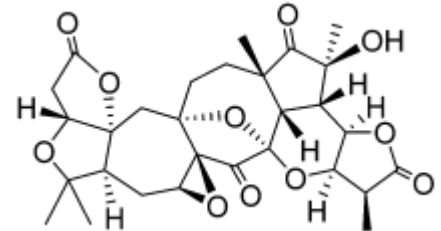
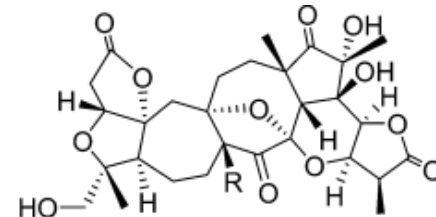
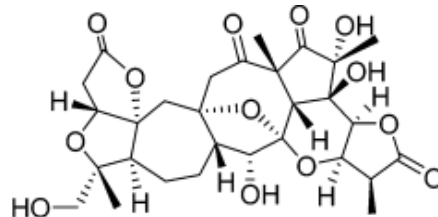
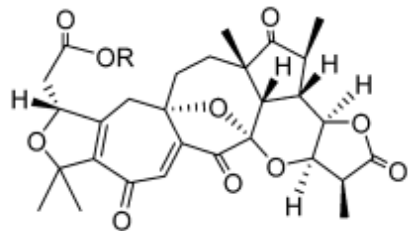
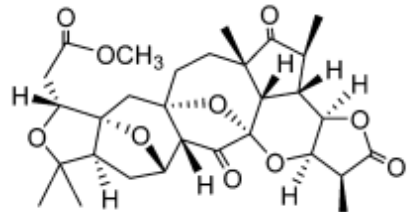
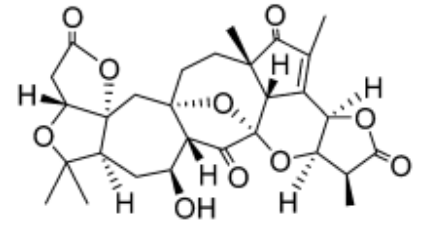
R ₁	R ₂	R ₃	R ₄
CH ₃	OH	OH	H
CH ₃	OH	H	H
OH	CH ₃	H	H
CH ₃	H	H	H
H	CH ₃	H	OH
CH ₃	H	H	OH
H	CH ₃	H	H



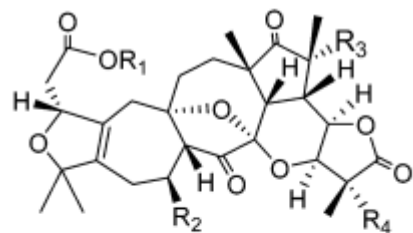
R ₁	R ₂	R ₃	R ₄
OH	CH ₃	H	H
CH ₃	H	H	H
CH ₃	H	H	OH
CH ₃	OH	H	H
CH ₃	OH	OH	H
CH ₃	H	H	H



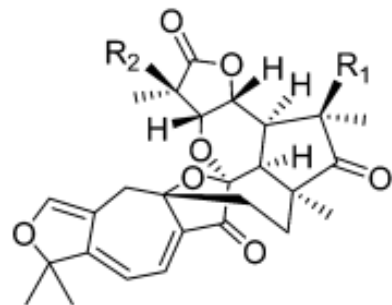
lancifodilactone G,
EC₅₀ 95.5 μg/mL



1. Background

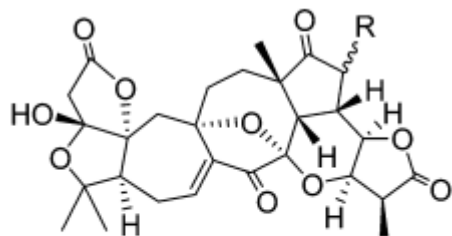
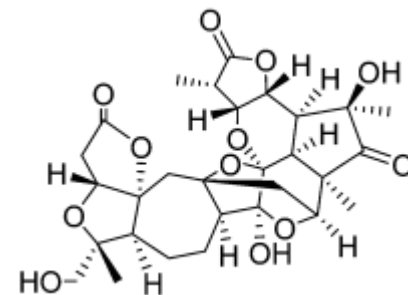
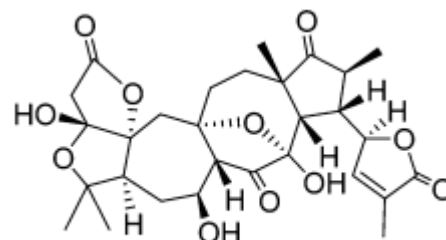
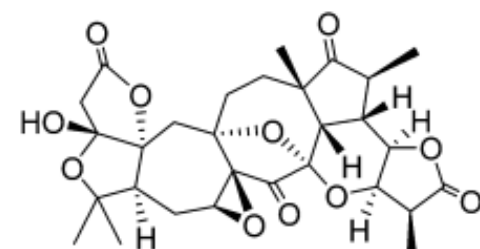
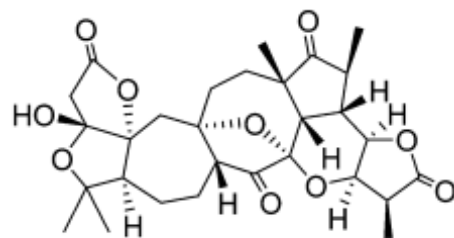


R ₁	R ₂	R ₃	R ₄
H	OH	H	H
H	OAc	H	H
H	OAc	H	OH
C ₂ H ₅	OH	H	H
C ₂ H ₅	OH	H	OH
C ₂ H ₅	OH	OH	OH
CH ₃	OH	H	H

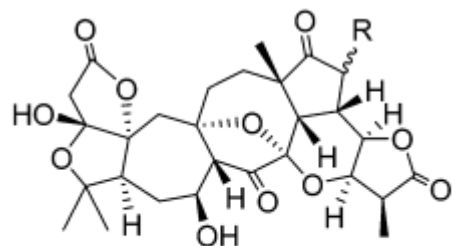


R₁ = OH, R₂ = H
 R₁ = H, R₂ = OH
 R₁ = OH, R₂ = OH
 R₁ = H, R₂ = H

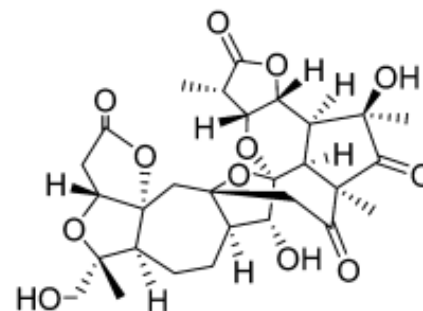
EC₅₀ 35.5–137.0 μg/mL, low
 C8166 cells cytotoxicity



R = β-CH₃
 R = α-CH₃



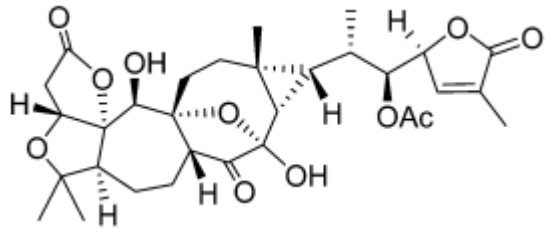
R = β-CH₃
 R = α-CH₃



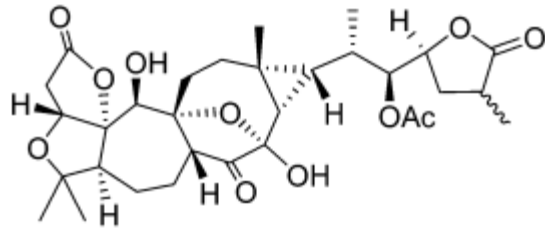
1. Background

1.2 Triterpenoids from the Schisandraceae family :

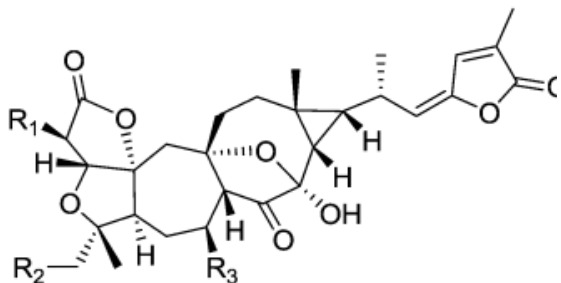
1.2.6. Pre-schisanartane-type



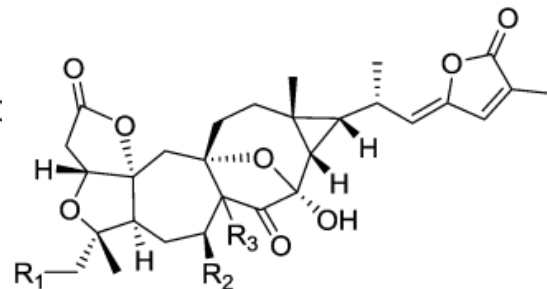
pre-schisanartanin A



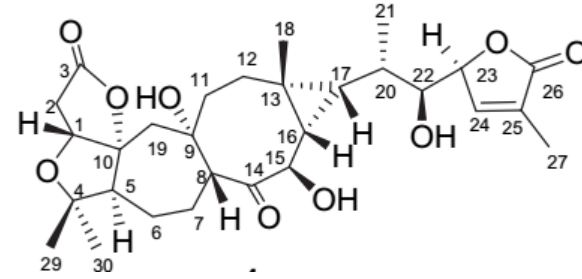
pre-schisanartanin B



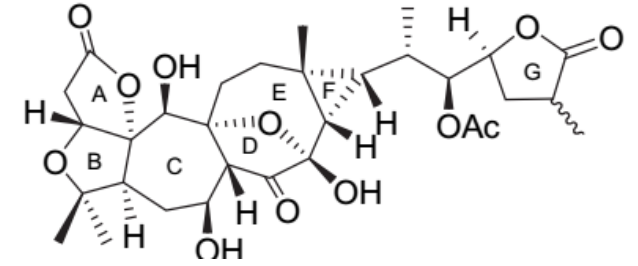
	R ₁	R ₂	R ₃
E	H	H	OH
H	H	OH	H
N	OH	H	OH



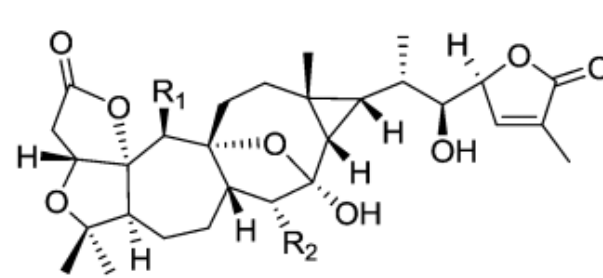
	R ₁	R ₂	R ₃
F	H	OH	β -H
G	OH	H	α -H
I	OH	H	β -H



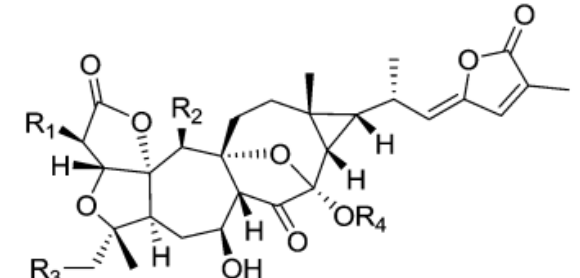
pre-schisanartanin C



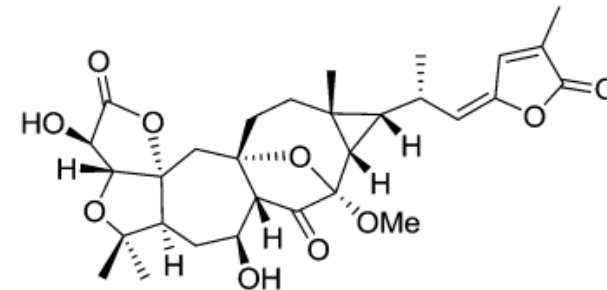
pre-schisanartanin D



J	R ₁ = H, R ₂ = OH
O	R ₁ = OH, R ₂ = =O



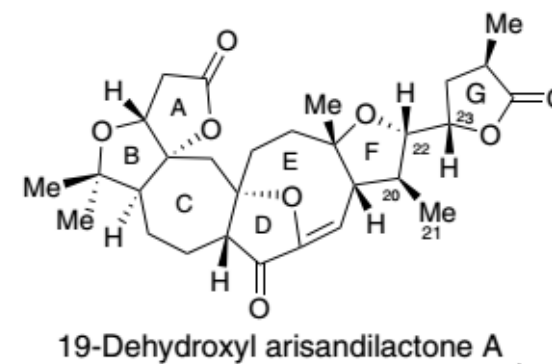
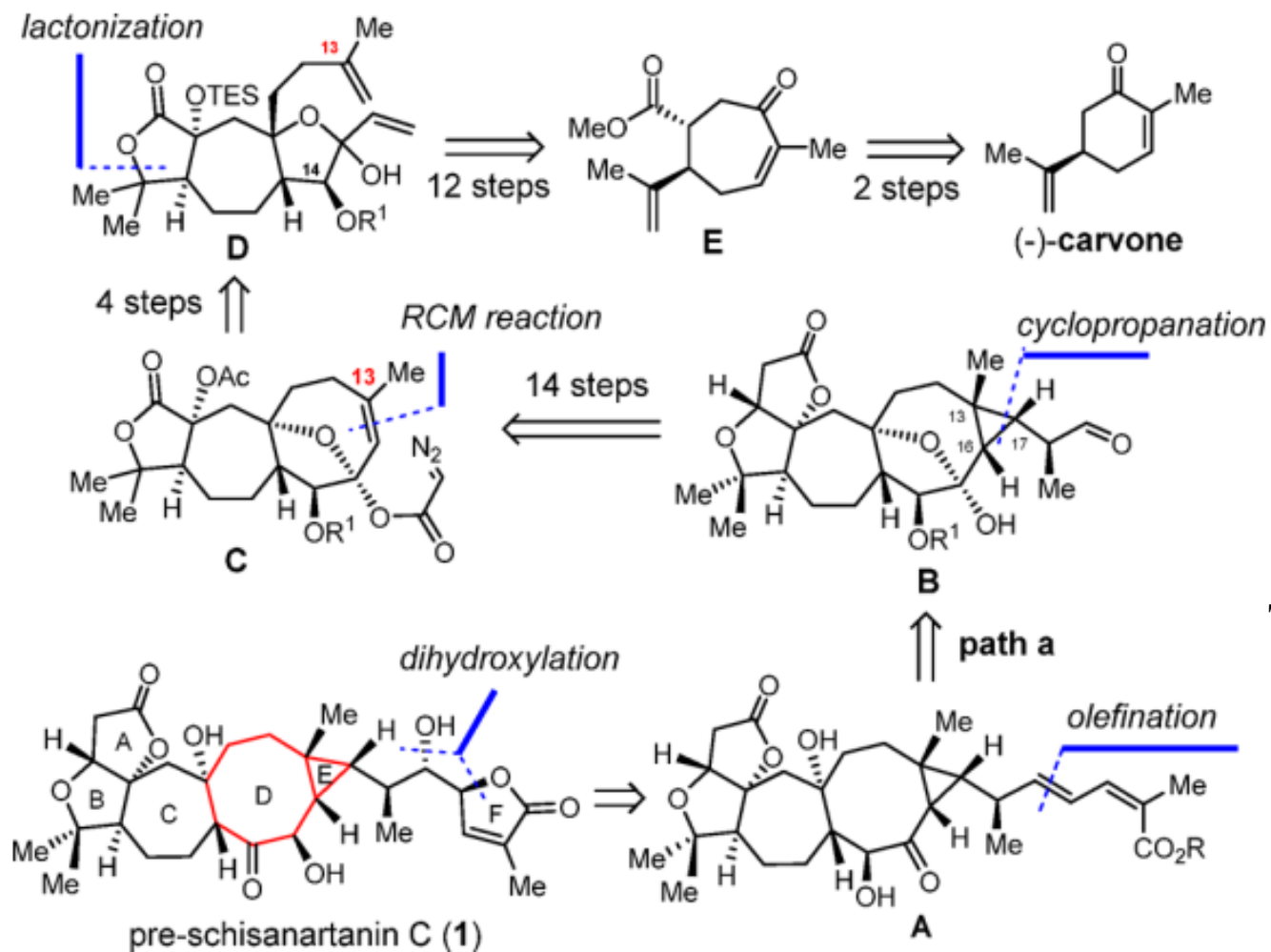
	R ₁	R ₂	R ₃	R ₄
K	H	OH	H	H
L	H	H	OH	Me



M

2. Total Synthesis of Pre-schisanartanin C

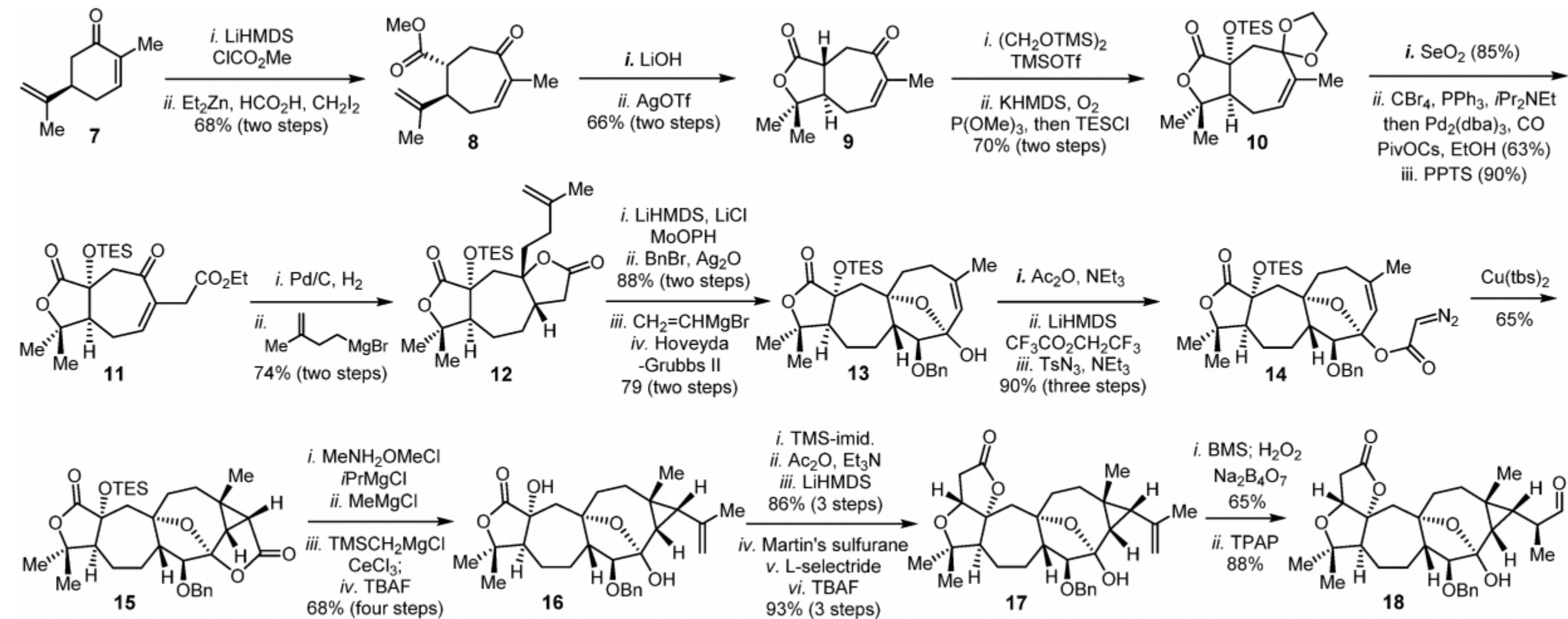
2.1. Retrosynthetic analysis of pre-schisanartanin C - path a



This strategy got (+)-19-dehydroxyl arisandilactone A

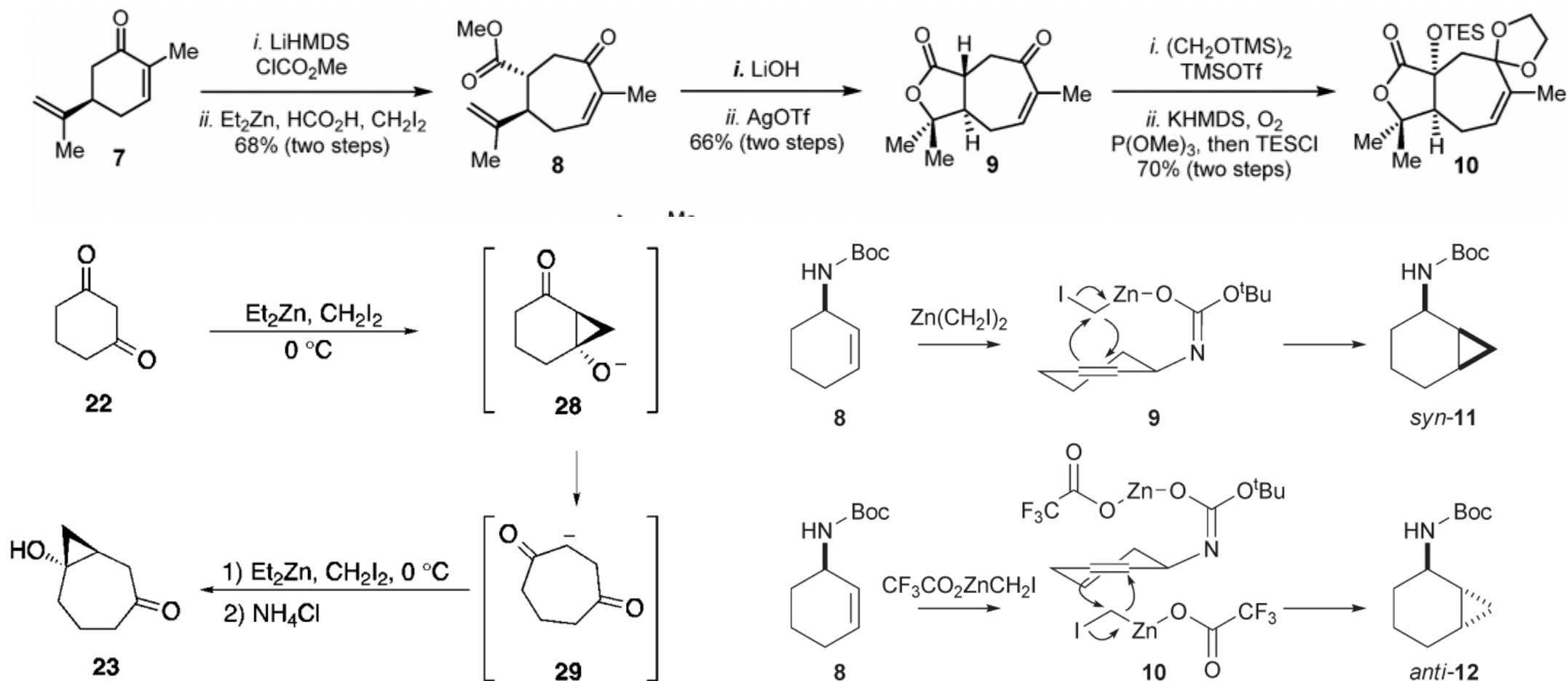
2. Total Synthesis of Pre-schisanartanin C

2.1.1 First strategy got (+)-19-dehydroxyl arisandilactone A



2. Total Synthesis of Pre-schisanartanin C

2.1.1 First strategy got (+)-19-dehydroxyl arisandilactone A

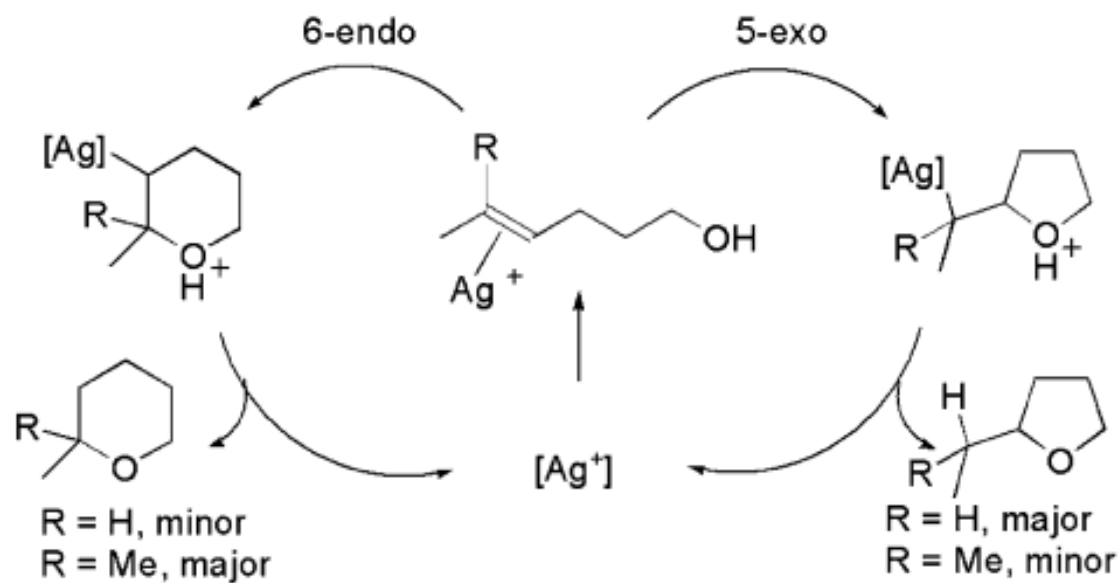
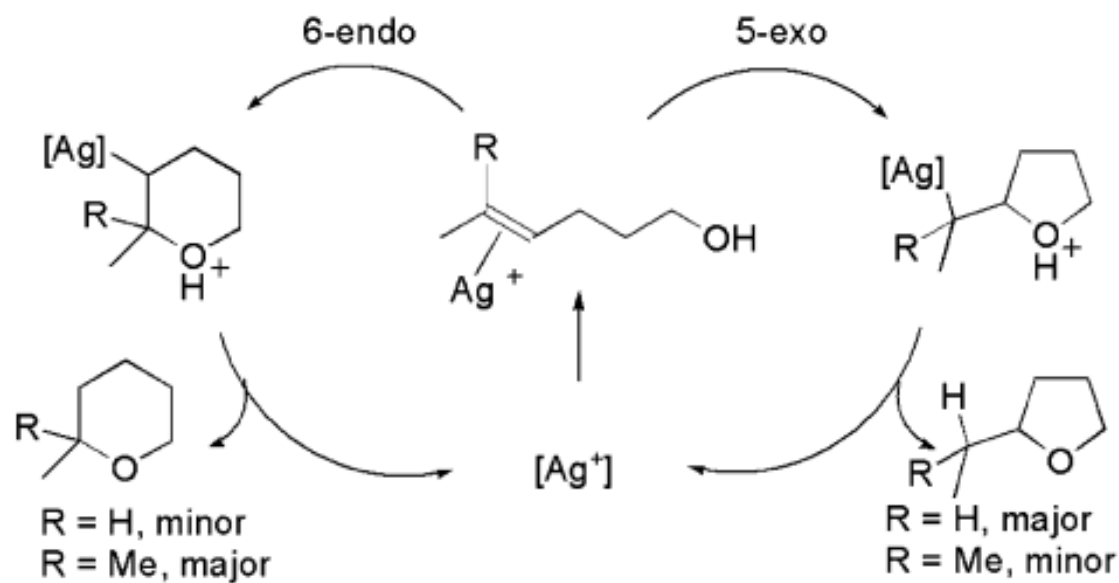
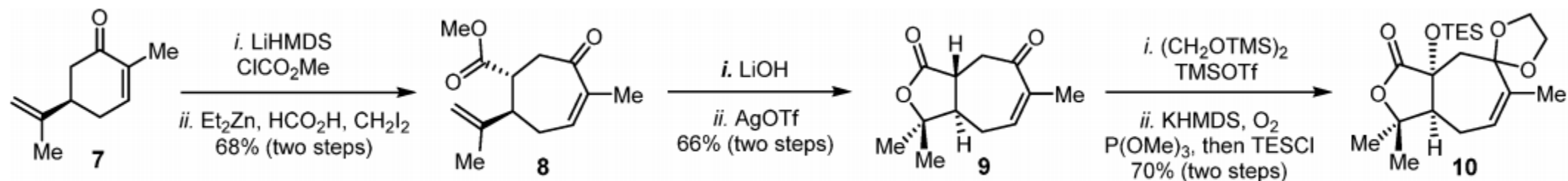


Charles K. Zercher, *J. Org. Chem.* **1997**, *62*, 6444

Stephen G. Davies, *Chem. Commun.*, 2007, 4029

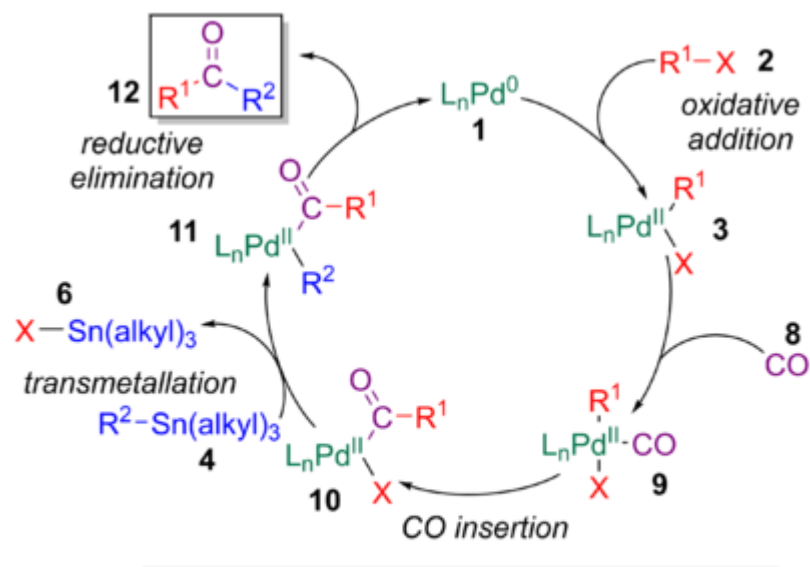
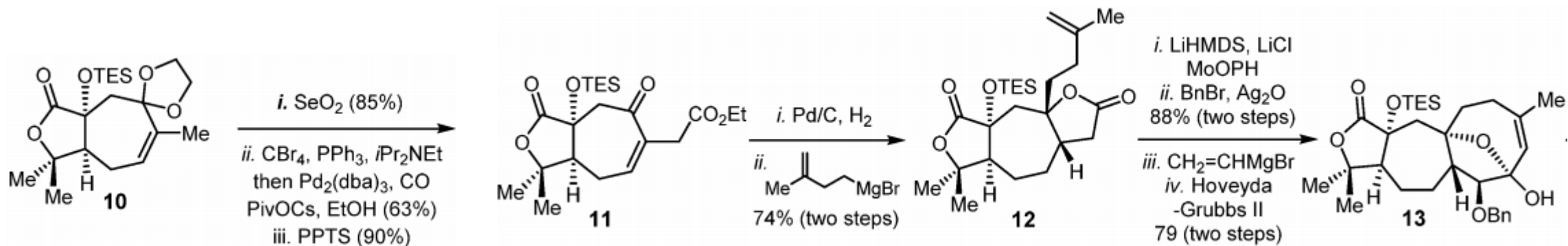
2. Total Synthesis of Pre-schisanartanin C

2.1.1 First strategy got (+)-19-dehydroxyl arisandilactone A

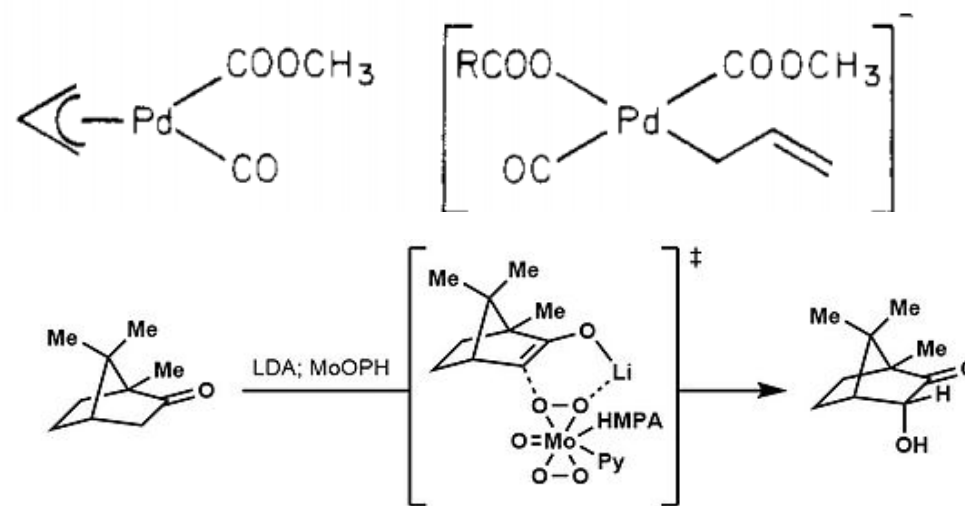


2. Total Synthesis of Pre-schisanartanin C

2.1.1 First strategy got (+)-19-dehydroxyl arisandilactone A

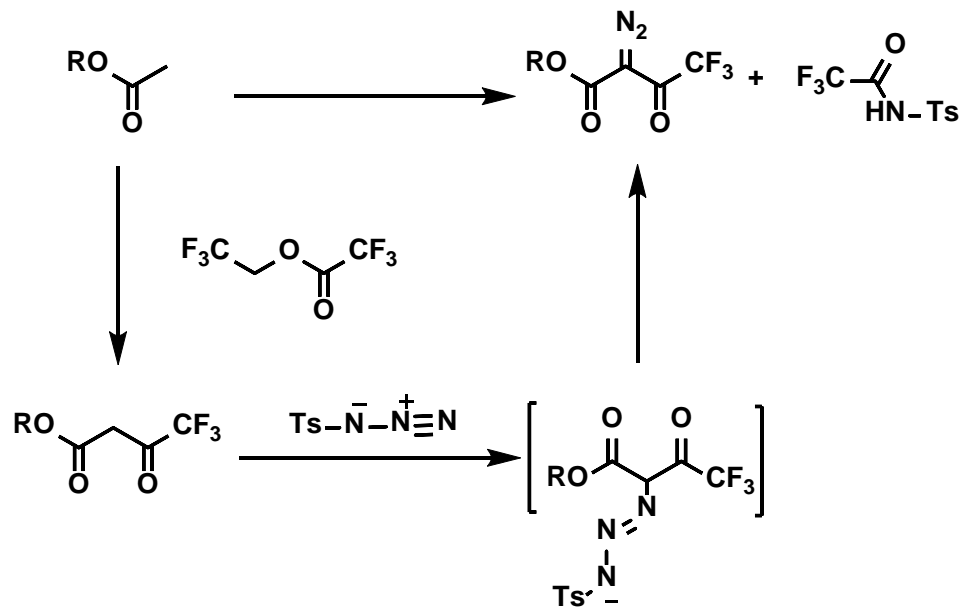
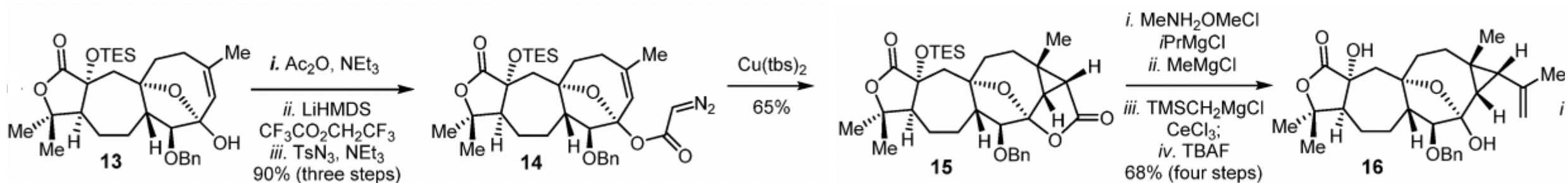


R^1, R^2 = allyl, alkenyl, aryl; X = Cl, Br, I, OTf, etc.
 L = phosphine; alkyl = Me, Bu



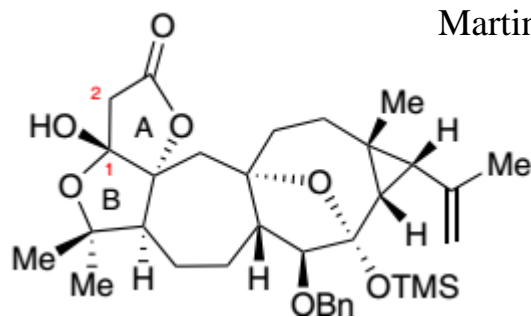
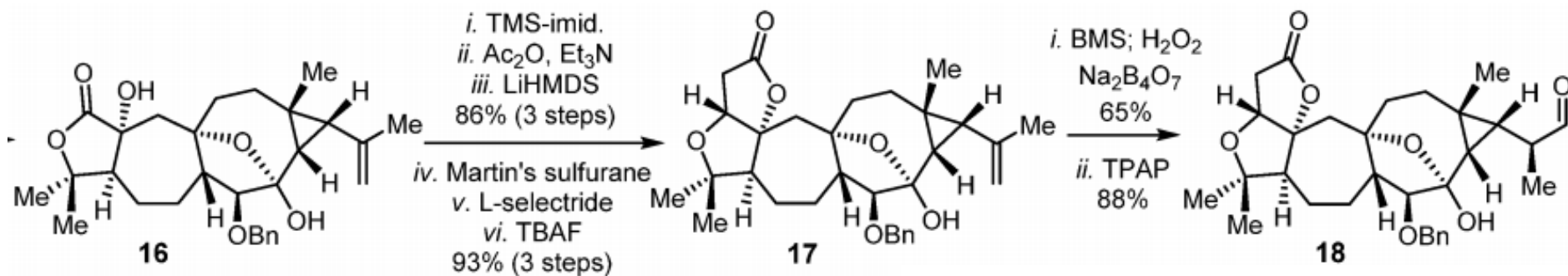
2. Total Synthesis of Pre-schisanartanin C

2.1.1 First strategy got (+)-19-dehydroxyl arisandilactone A

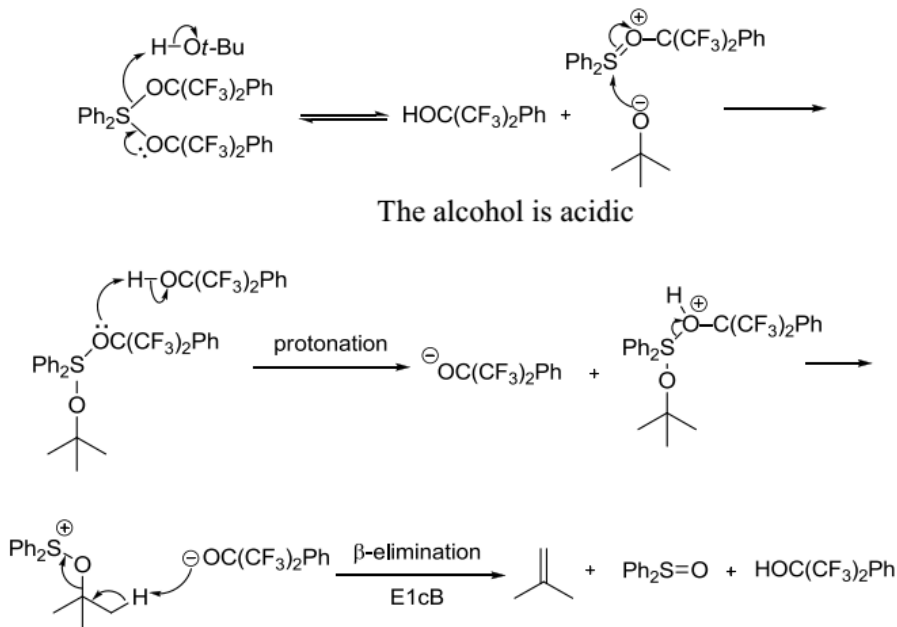


2. Total Synthesis of Pre-schisanartanin C

2.1.1 First strategy got (+)-19-dehydroxyl arisandilactone A



Dehydrates secondary and tertiary alcohols to give olefins, **but forms ethers with primary alcohols**

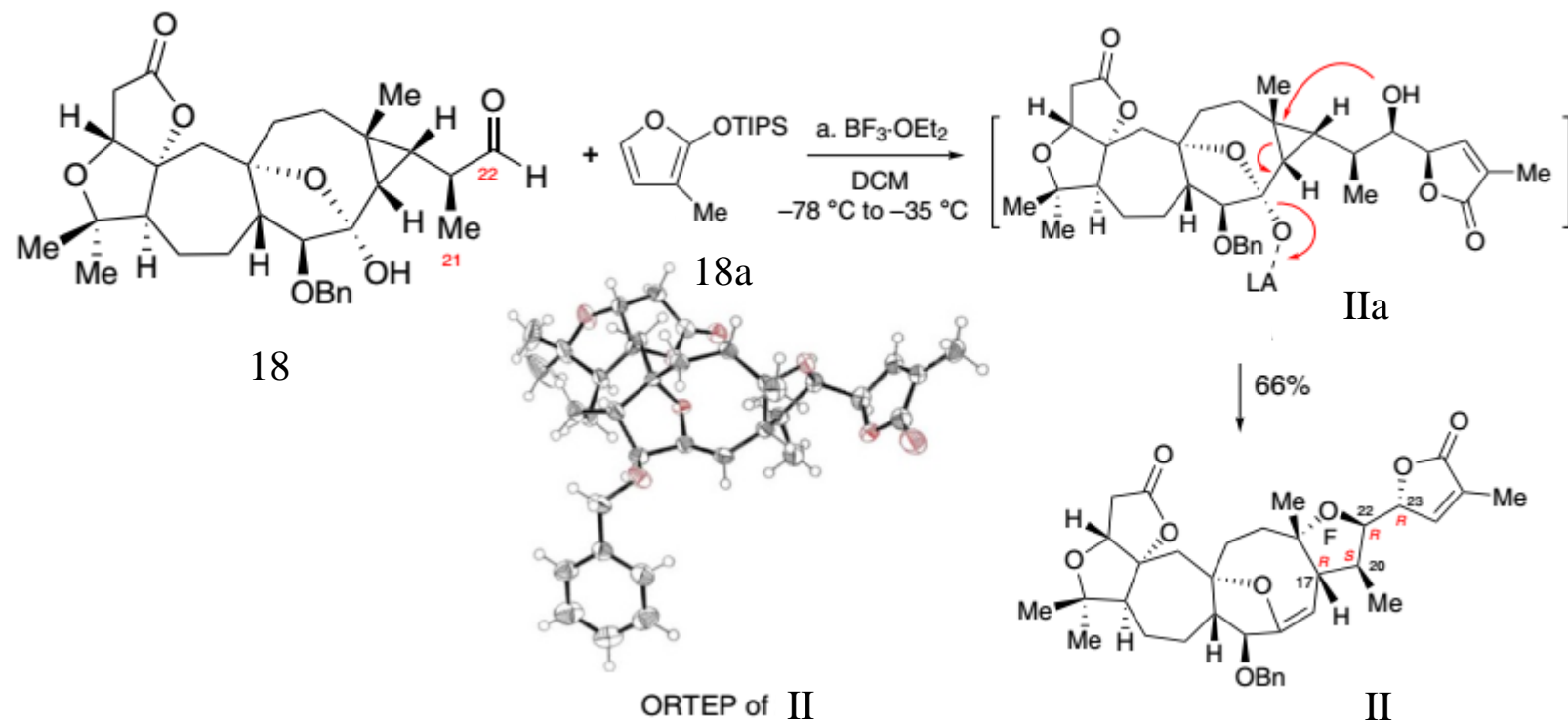


Martin's sulfurane dehydrating reagent



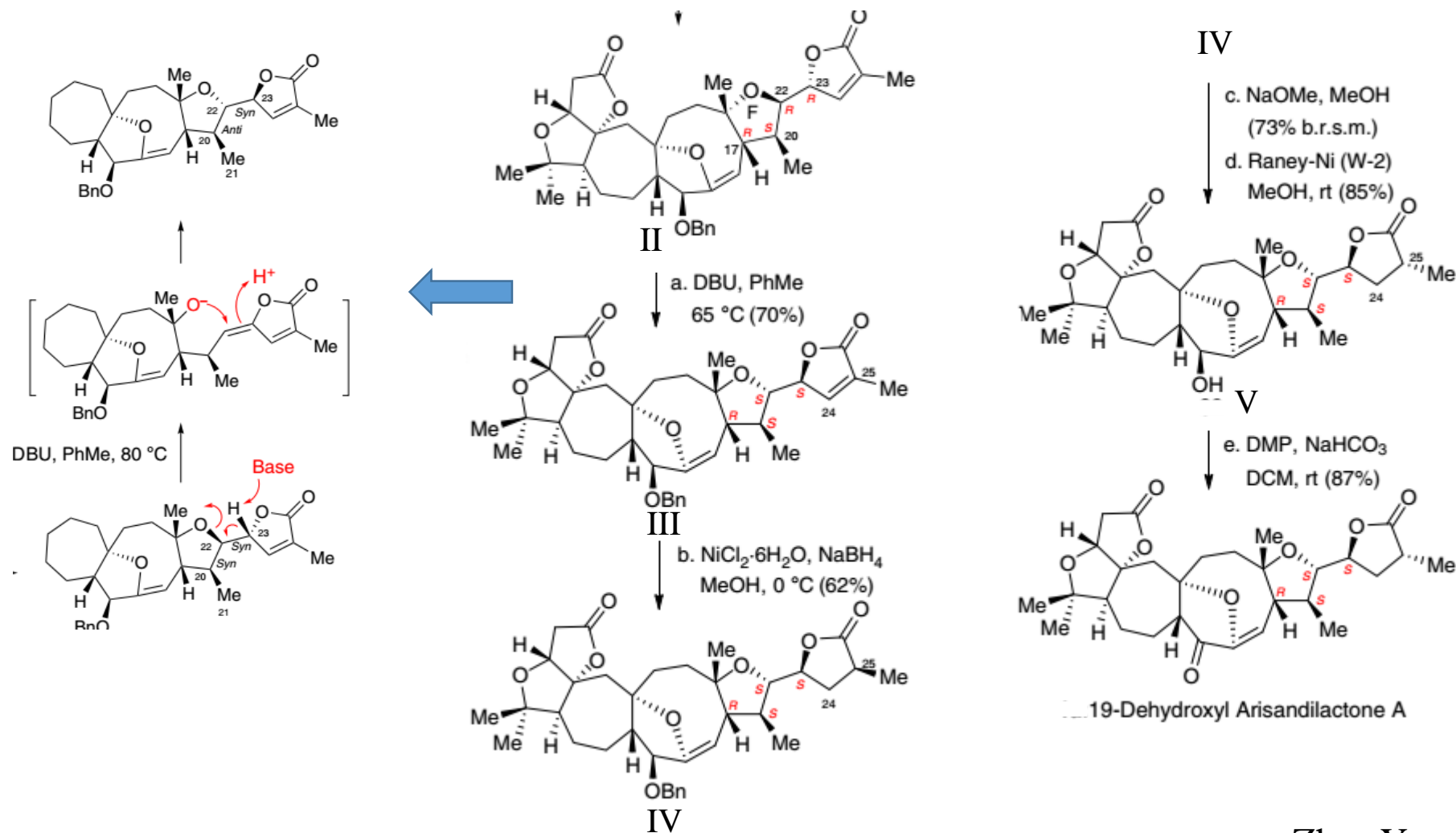
2. Total Synthesis of Pre-schisananartanin C

2.1.1 First strategy got (+)-19-dehydroxyl arisandilactone A



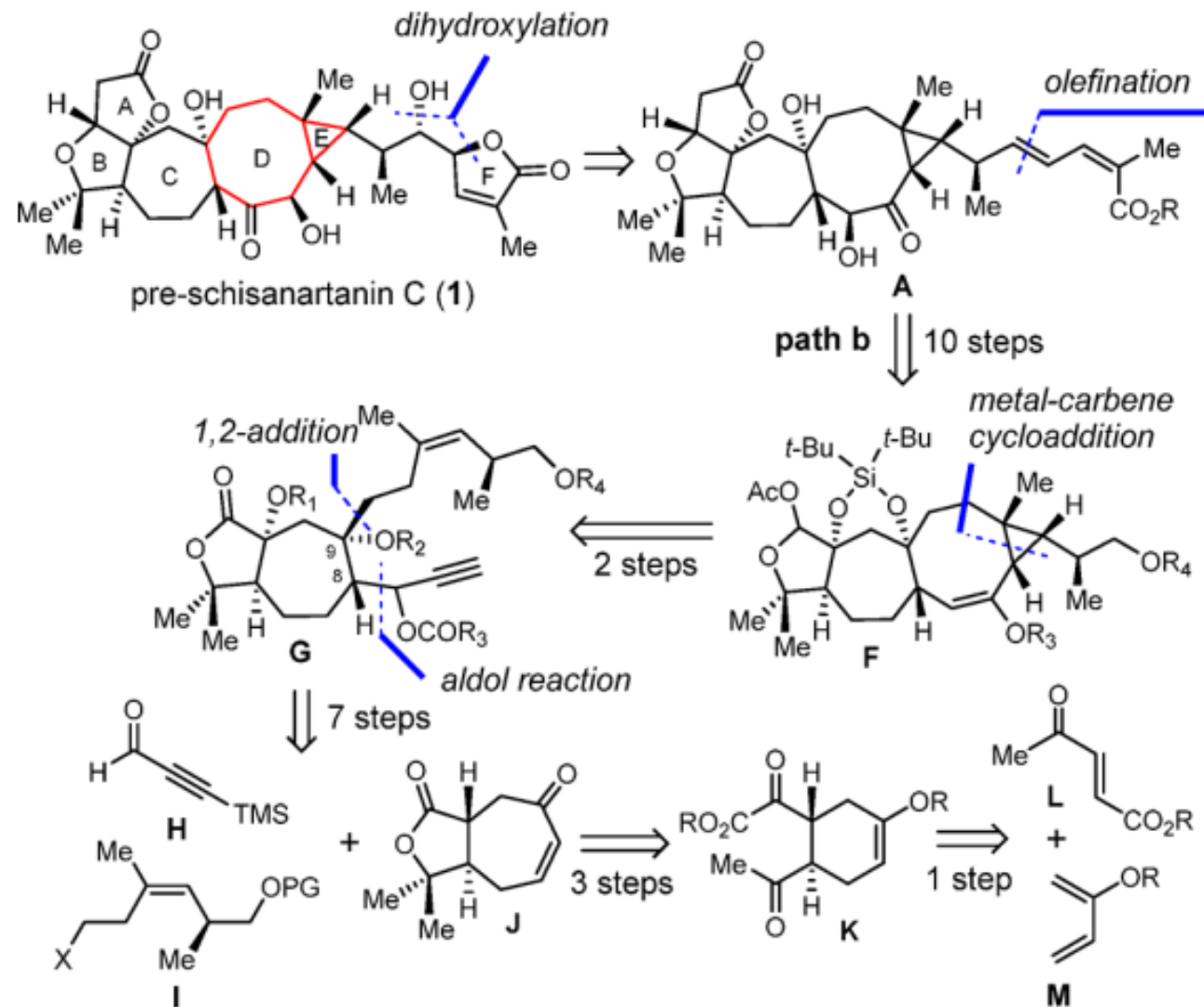
2. Total Synthesis of Pre-schisananartanin C

2.1.1 First strategy got (+)-19-dehydroxyl arisandilactone A



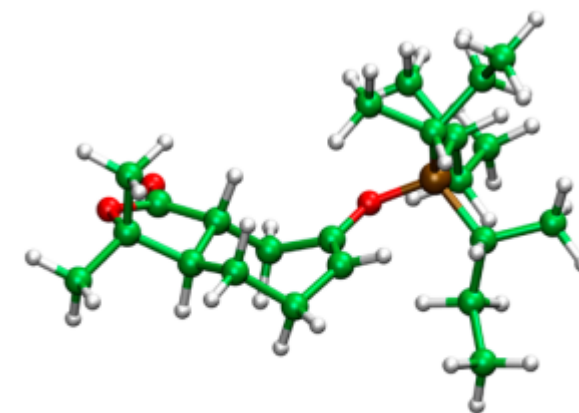
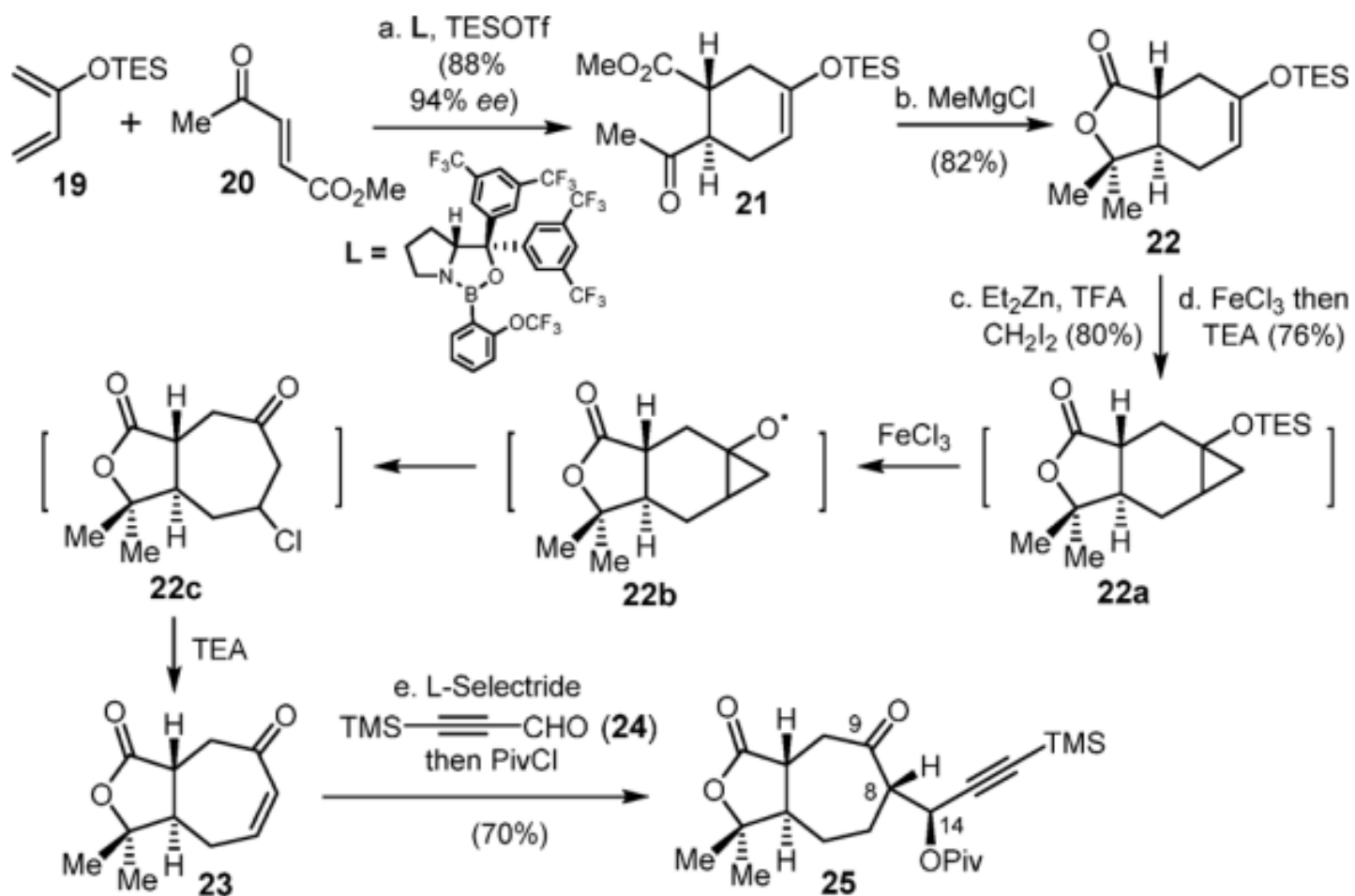
2. Total Synthesis of Pre-schisanartanin C

2.2. Retrosynthetic analysis of pre-schisanartanin C – path b

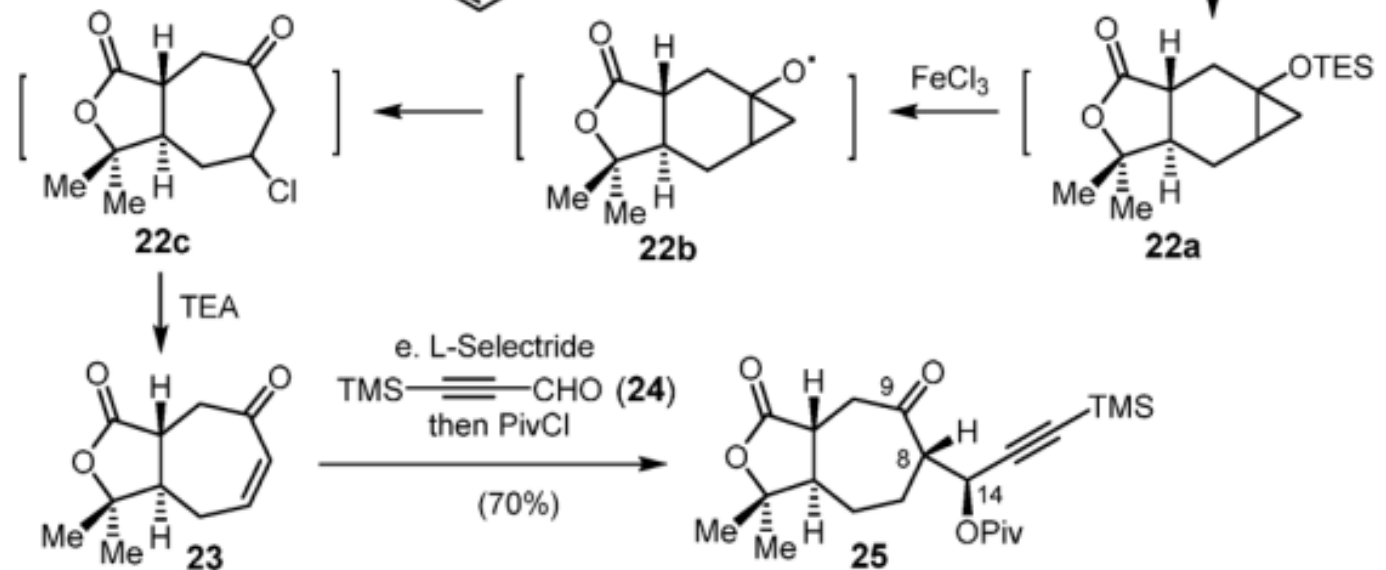


2. Total Synthesis of Pre-schisanartanin C

2.2.1. Details of the synthesis



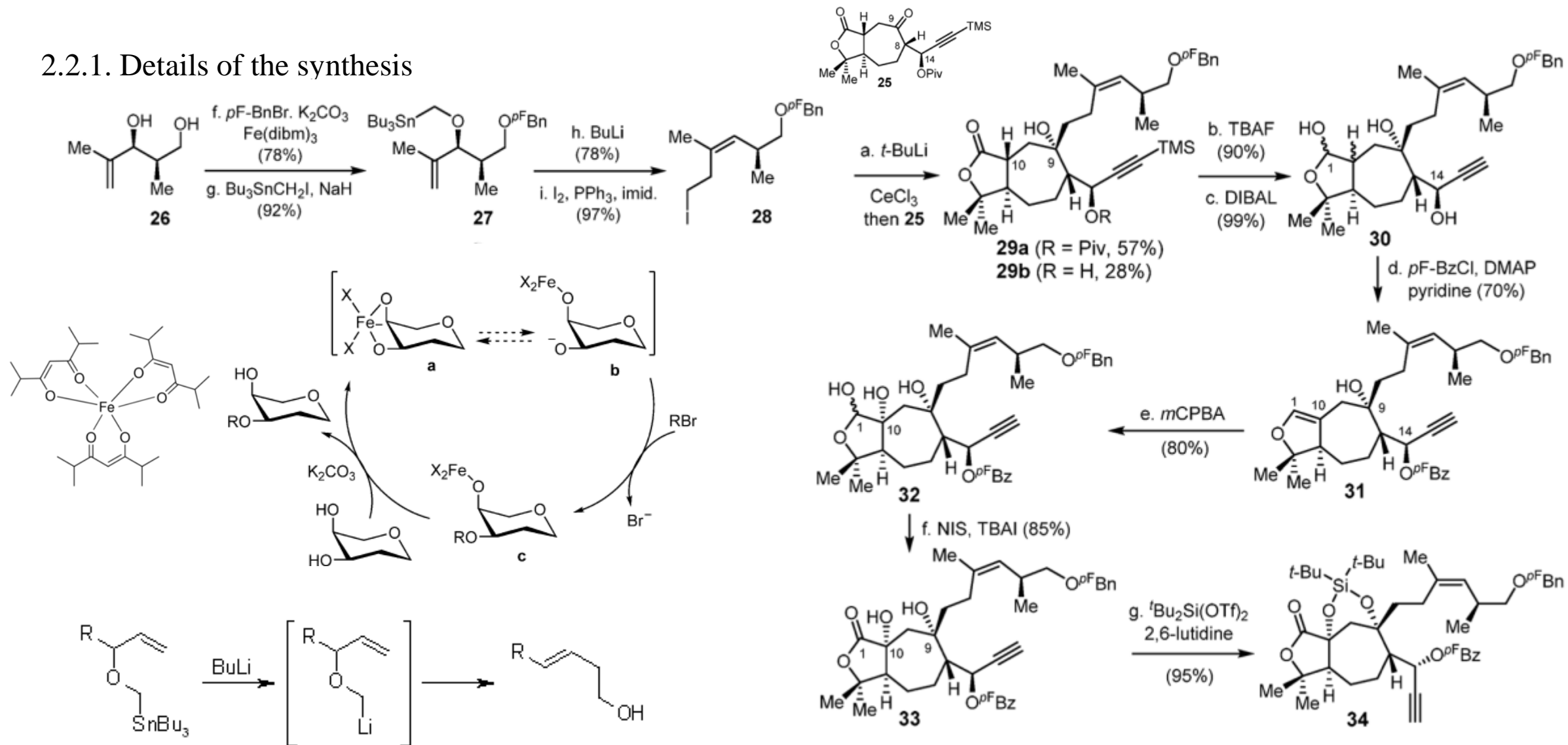
3D-structure of boran-enolate (A) derived from L-Selectride reduction of enone 23



proposed transition state (B) for the L-Selectride-mediated Aldol condensation

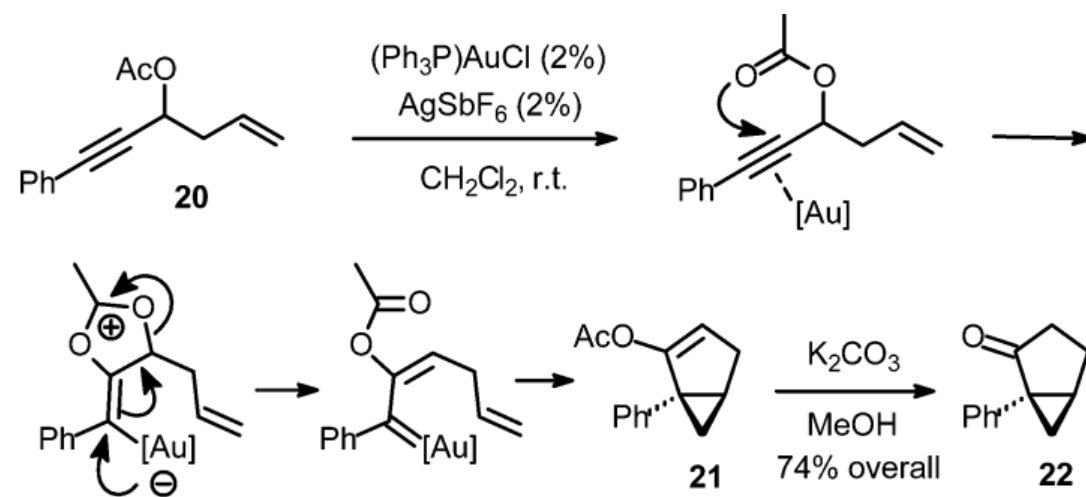
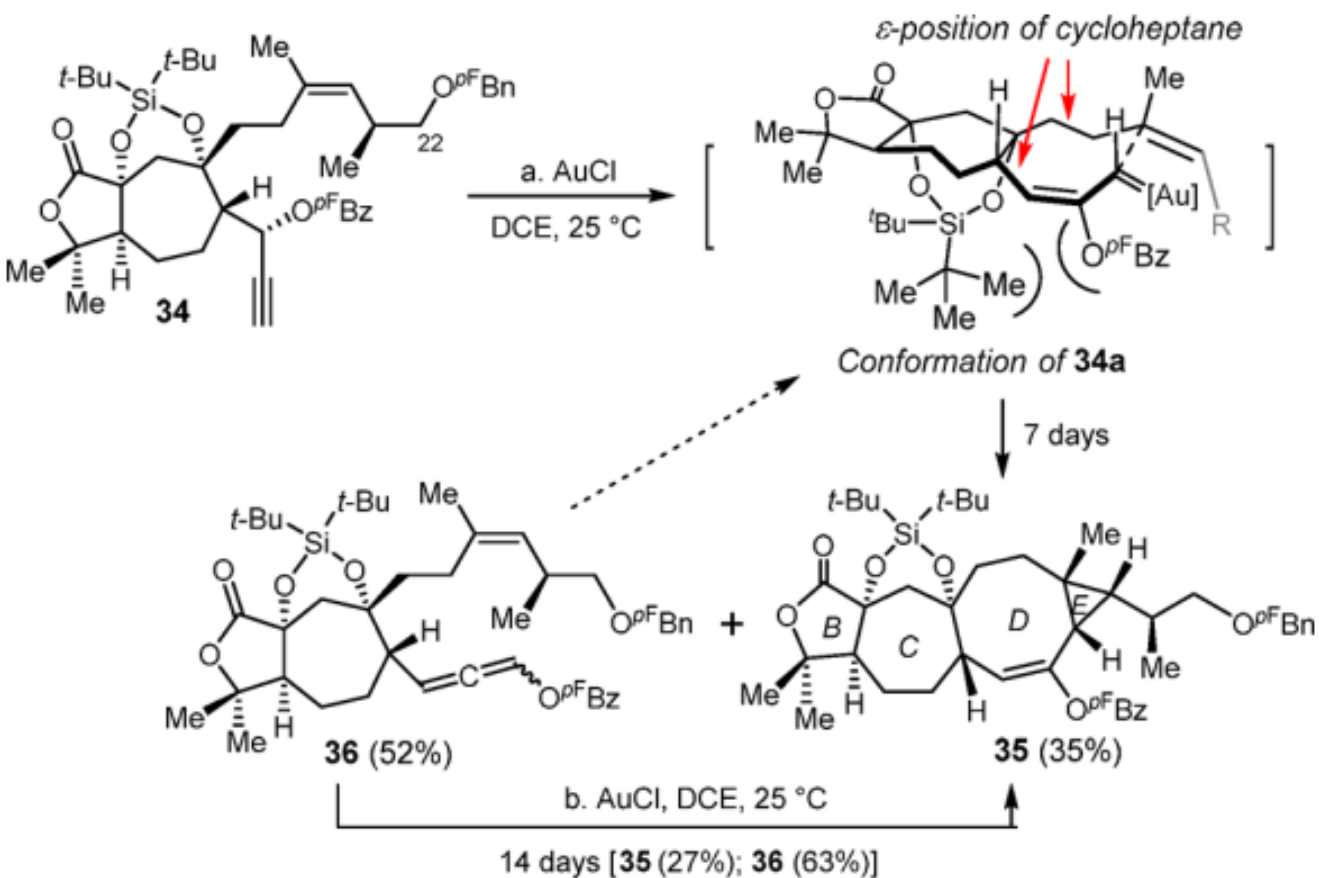
2. Total Synthesis of Pre-schisananartanin C

2.2.1. Details of the synthesis



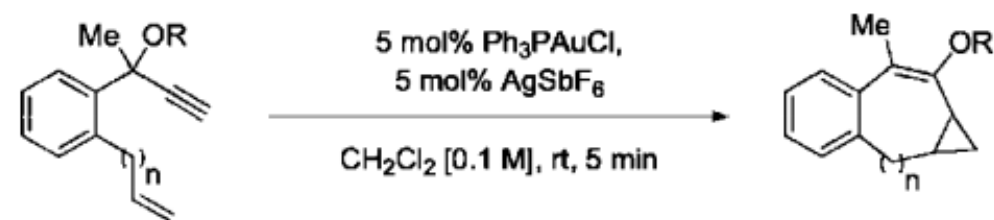
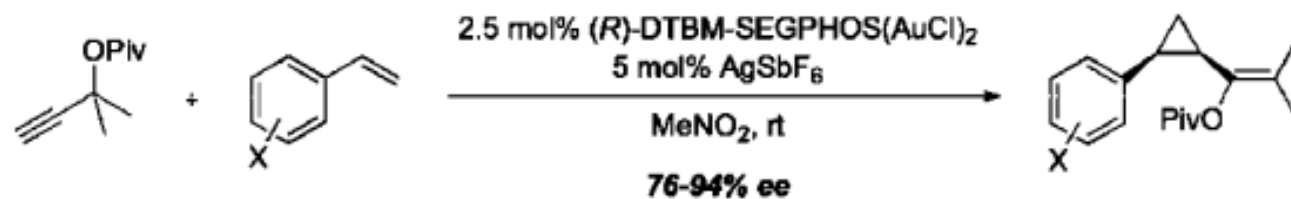
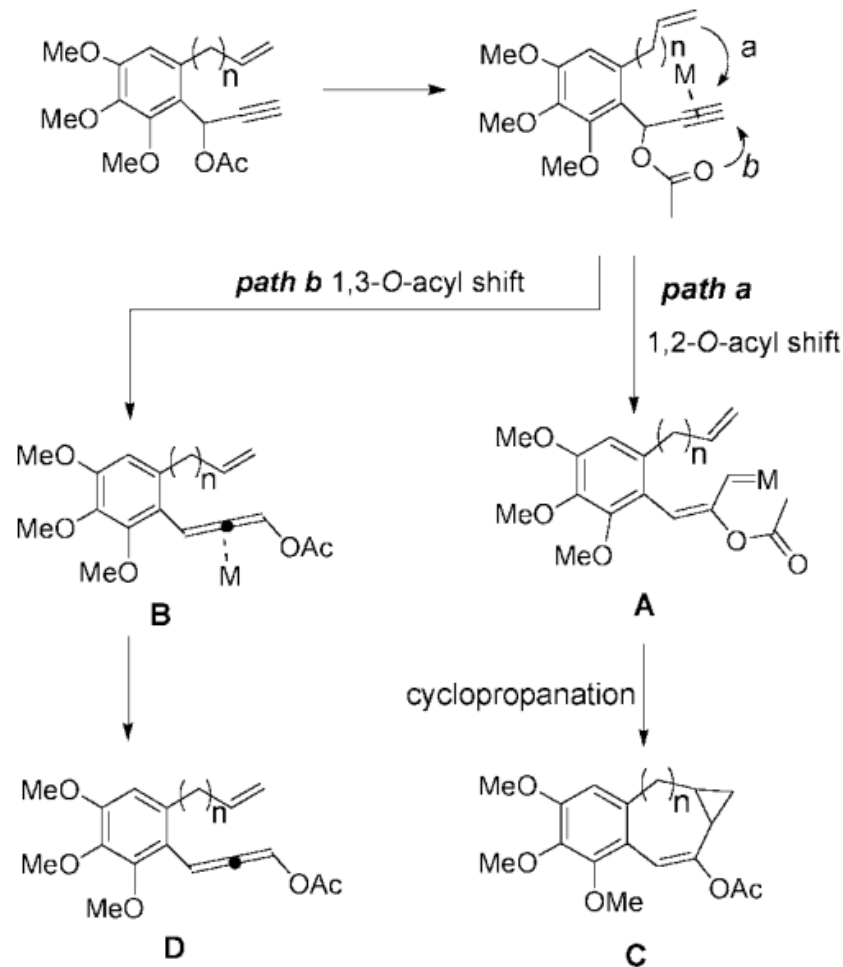
2. Total Synthesis of Pre-schisananartanin C

2.2.1. Details of the synthesis

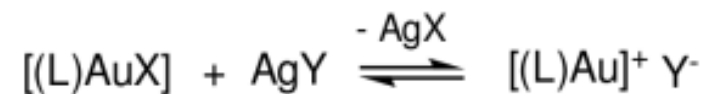


2. Total Synthesis of Pre-schisanartanin C

2.2.1. Details of the synthesis



1	$n = 0, R = \text{Ac}$	2	10%
3	$n = 1, R = \text{Piv}$	4	99%
5	$n = 2, R = \text{Piv}$	6	99%
7	$n = 3, R = \text{Ac}$	8	44%



$X = \text{Cl, Br}; Y = \text{BF}_4, \text{PF}_6, \text{SbF}_6, \text{OTf}$

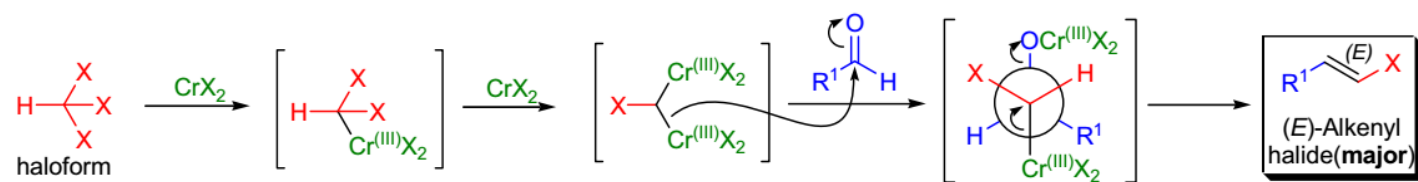
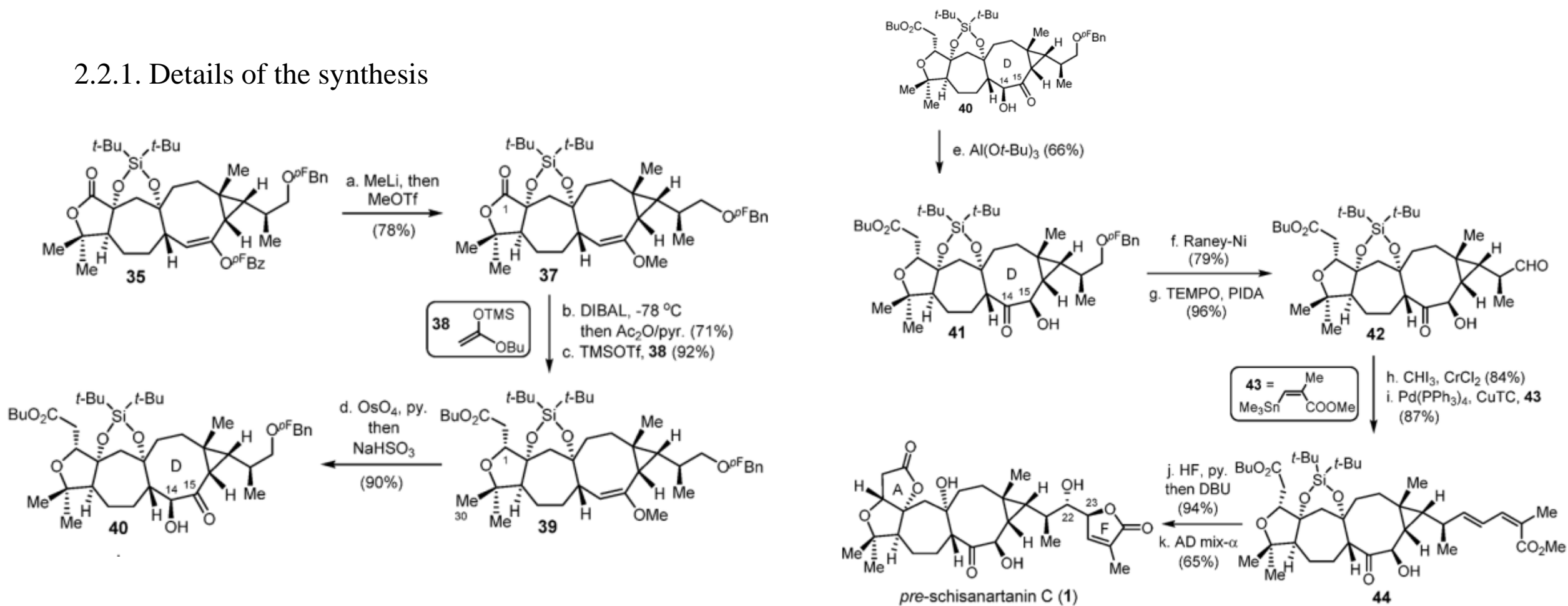
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2. Total Synthesis of Pre-schisanartanin C

2.2.1. Details of the synthesis



Takai-Utimoto olefination

Thanks for your attention !