Literature Report

Changbin Yu 2012-06-26 检查: Kai Gao

Total Syntheses of Anominine and Tubingensin A

Ang Li* *et al*. *J. Am. Chem. Soc*. **2012**, *134*, 8078−8081.

Research Interests

Divergent total synthesis of biologically active natural products based on biosynthetic hypothesis or privileged core structures
Desymmetrization strategy in natural product total synthesis
Ring strain-promoted reactions in natural product synthesis

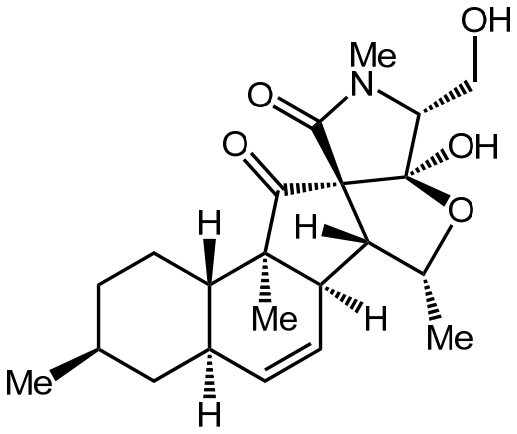
Professional Experience

2010–present "Bairen Jihua" Professor, Shanghai Institute of Organic Chemistry,
2010 Research fellow, Institute of Chemical and Engineering Sciences, Singapore
Advisor: Prof. K. C. Nicolaou

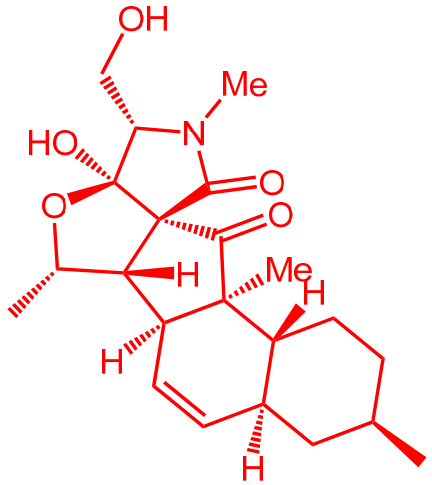
Education

2004–2009 Ph.D., The Scripps Research Institute
Advisor: Prof. K. C. Nicolaou
2000–2004 B.Sc., Peking University
Advisor: Prof. Zhen Yang

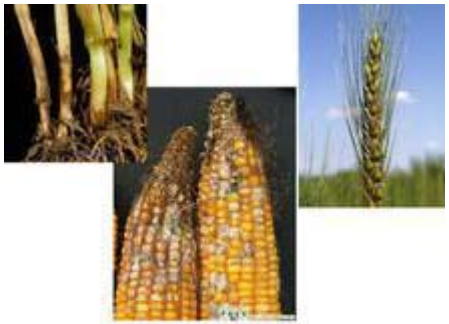
Structures of (-)-Fusarisetin A

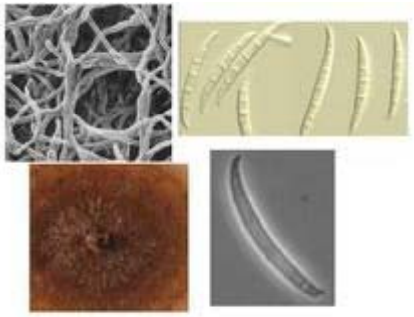


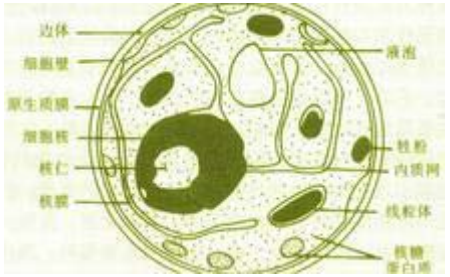
proposed structure of fusarisetin A



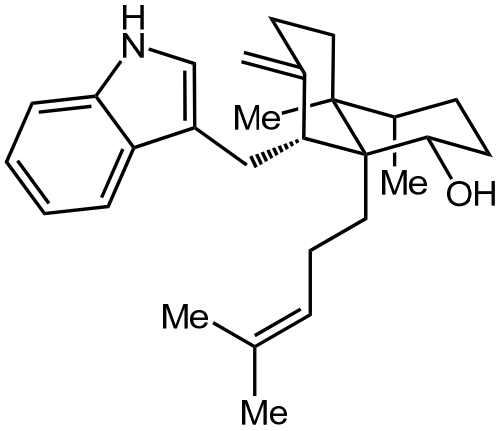
revised structure of fusarisetin A



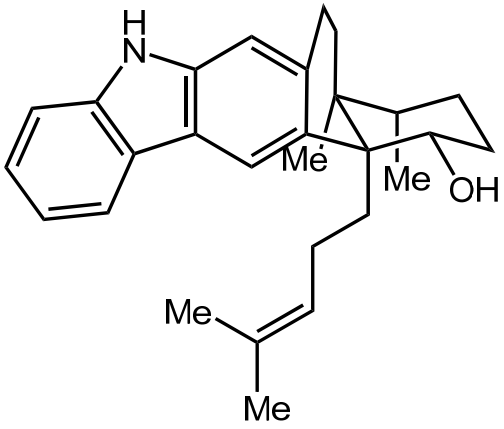




Structures of anominine and tubingensin A

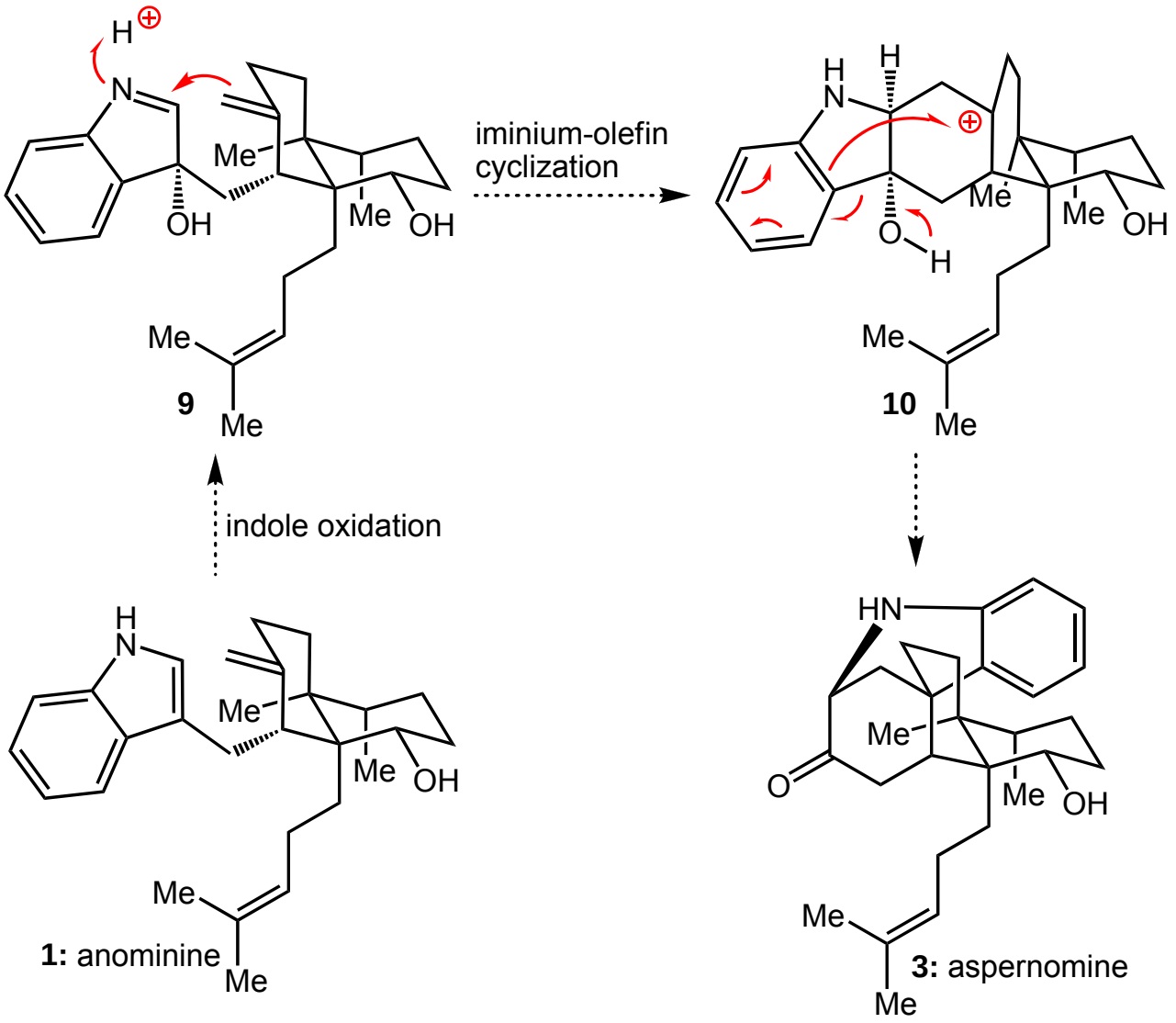


1: anominine

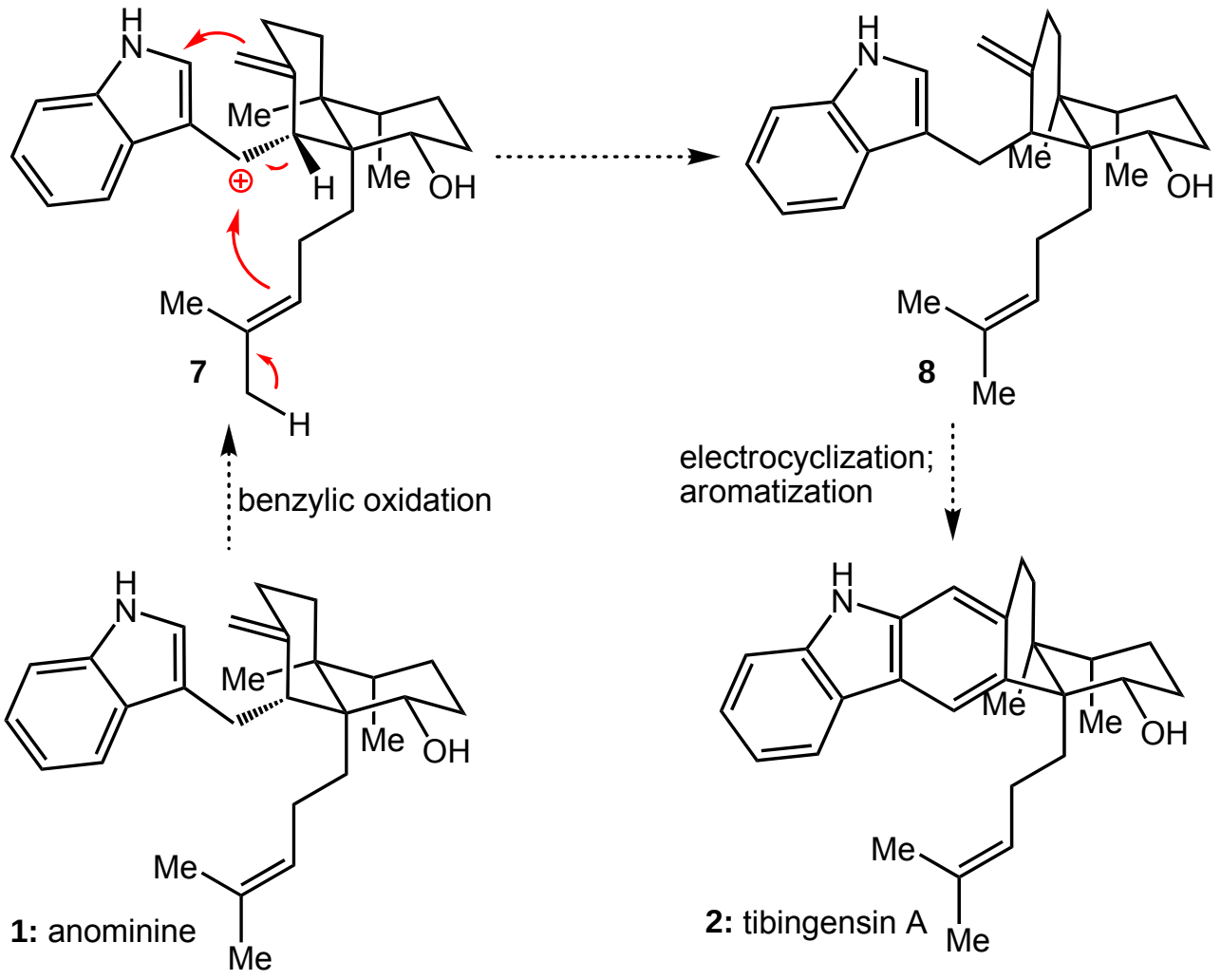


2: tubingensin A

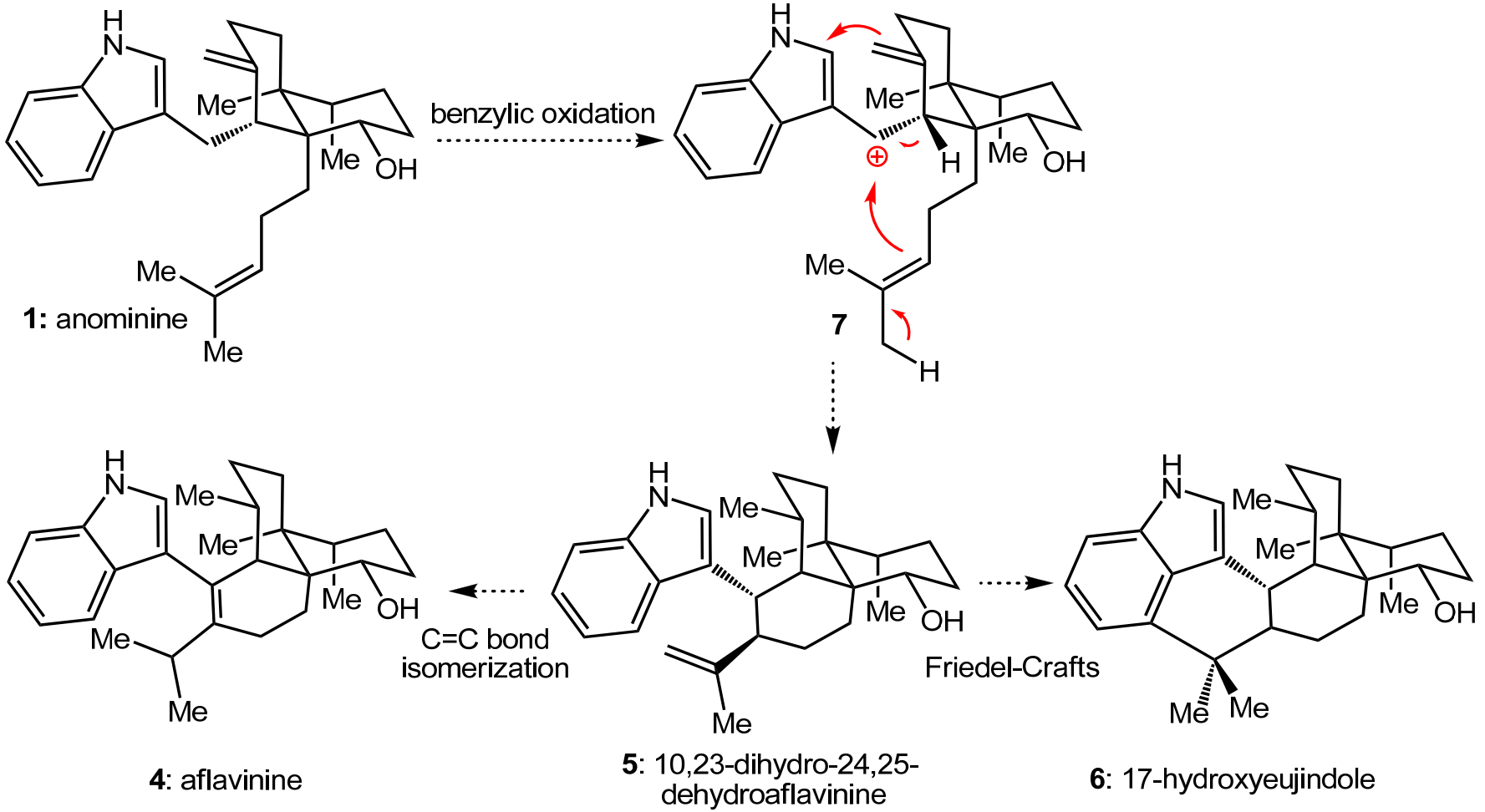
Postulated Biosynthetic Relationship among Some Members of the Anominine Family



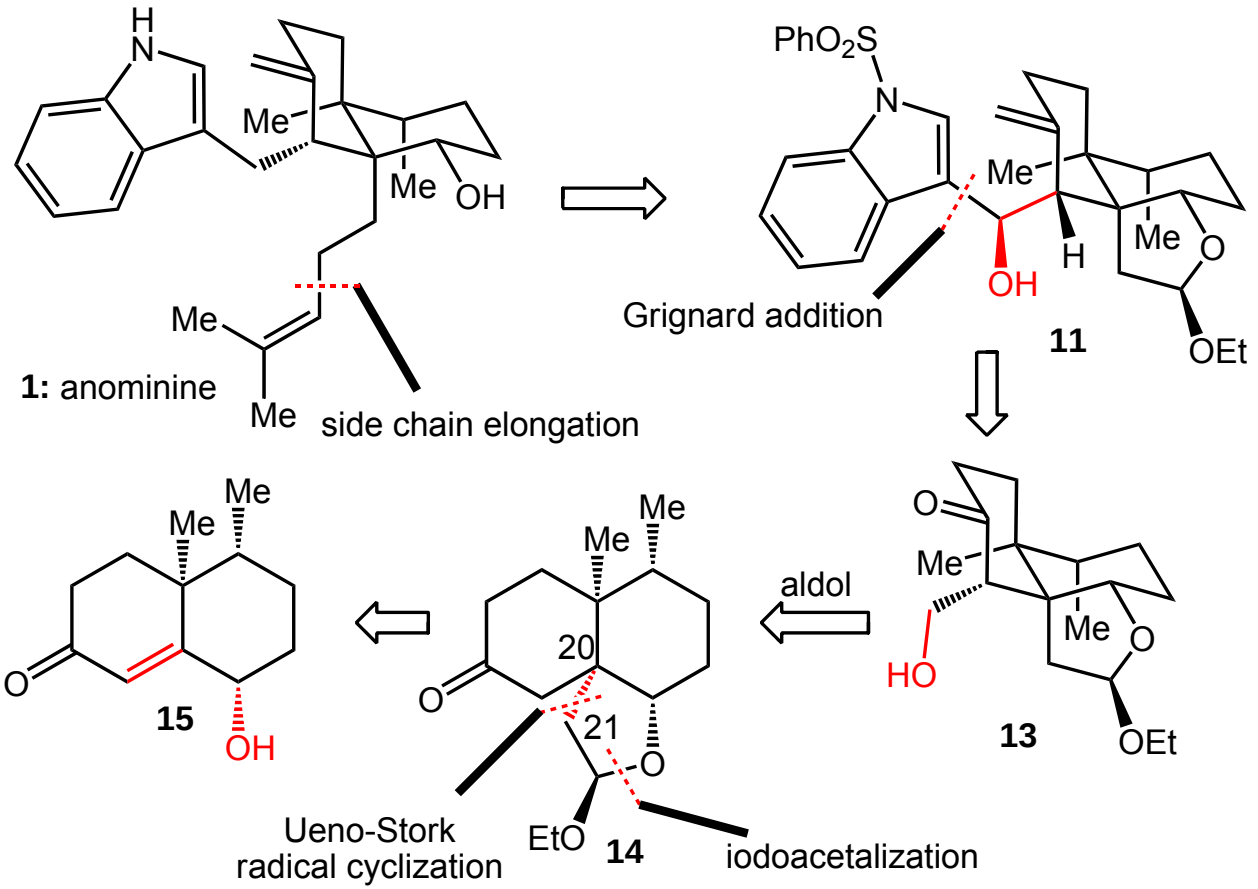
Postulated Biosynthetic Relationship among Some Members of the Anominine Family



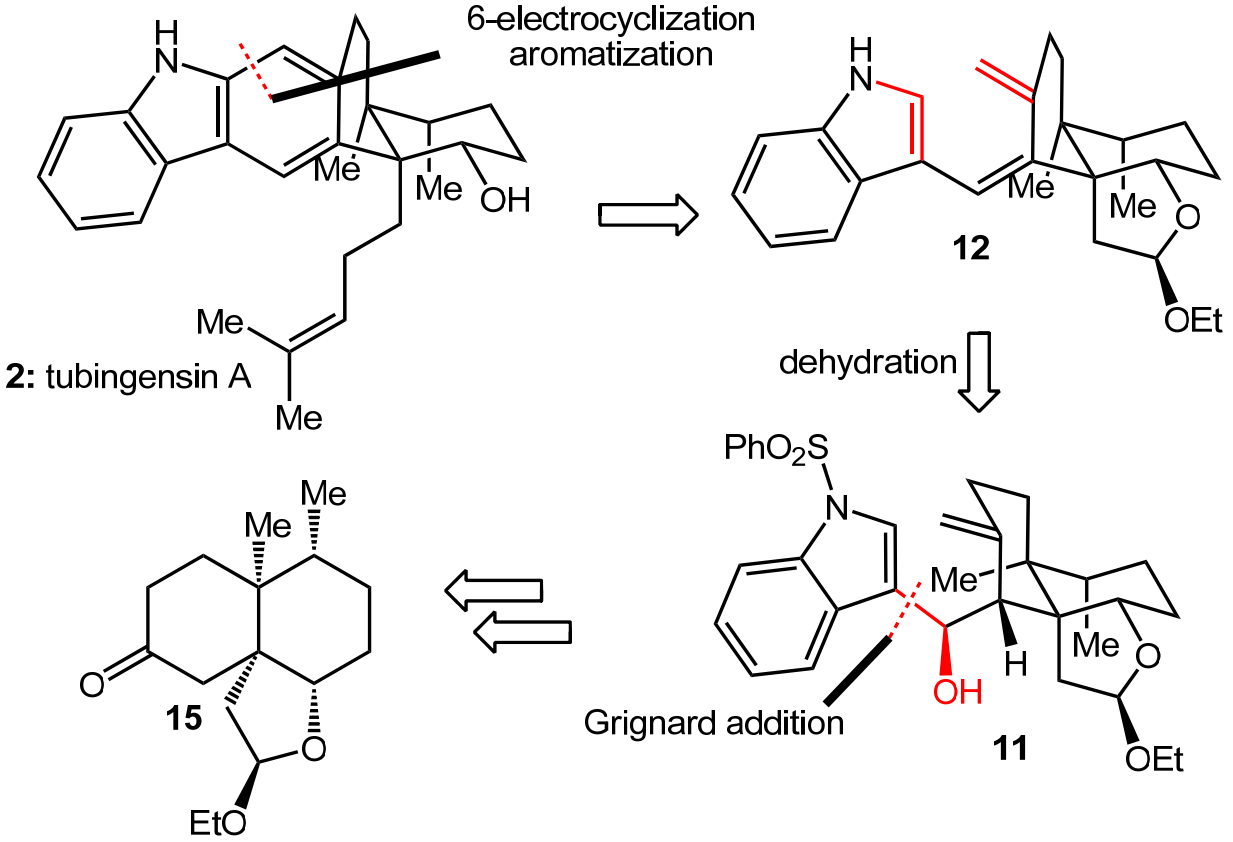
Postulated Biosynthetic Relationship among Some Members of the Anominine Family

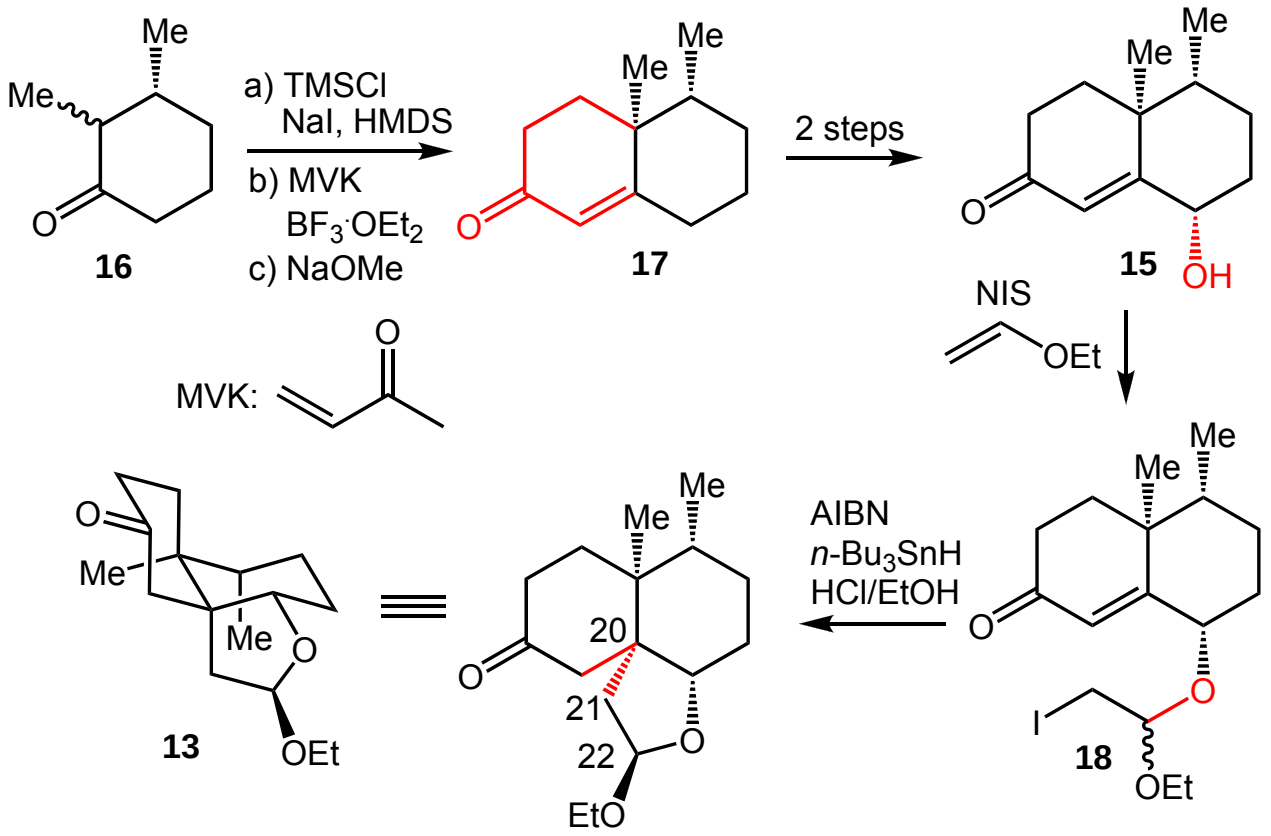


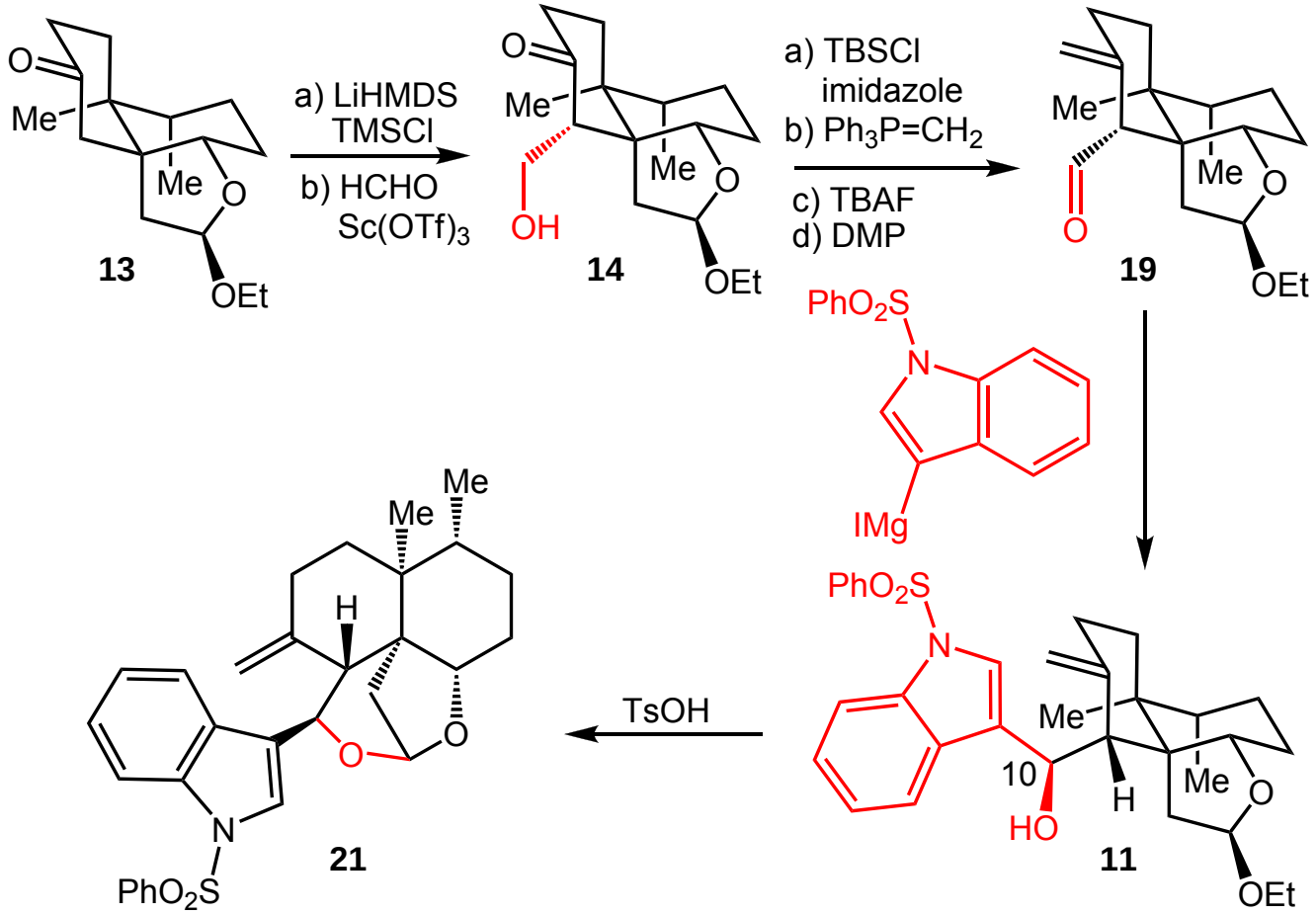
Retrosynthetic analysis of Anominine (**1**)

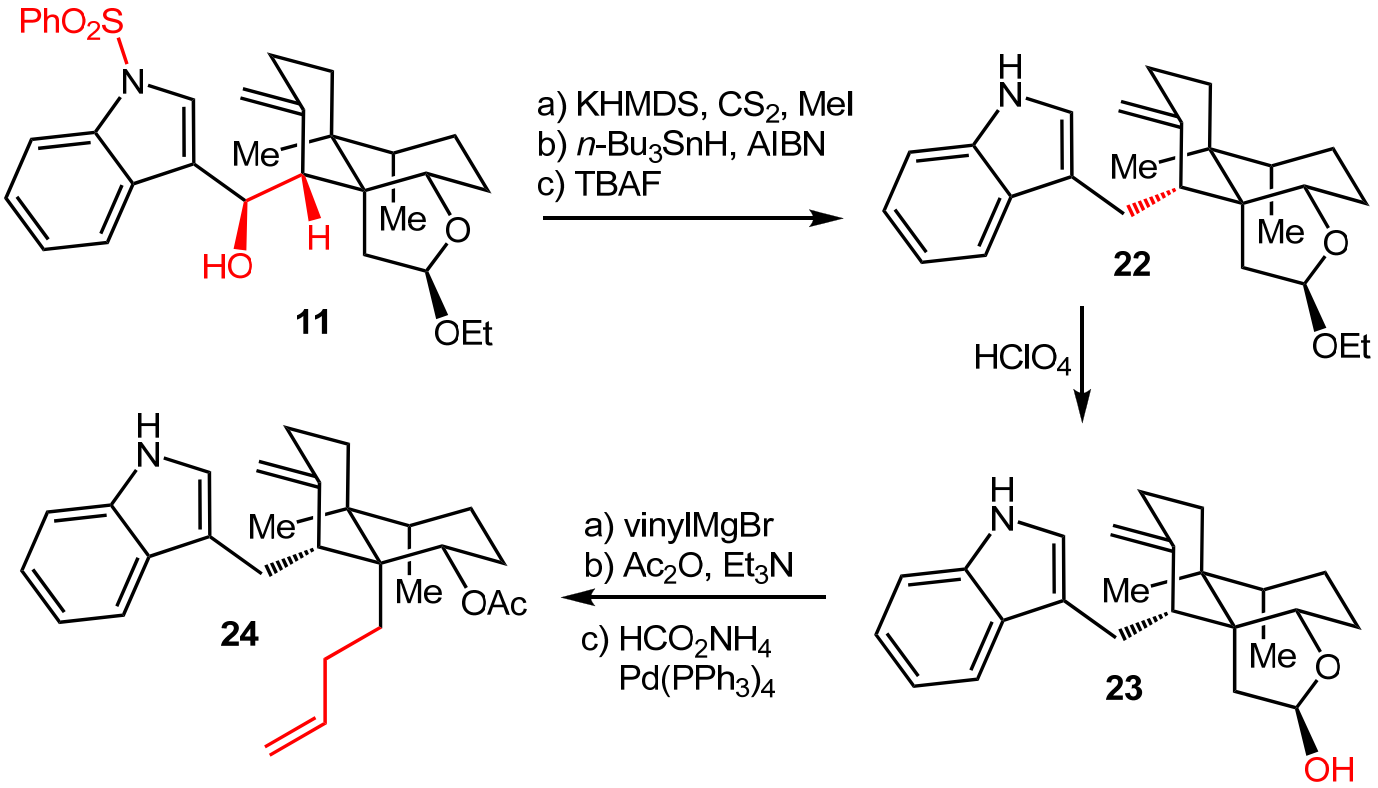


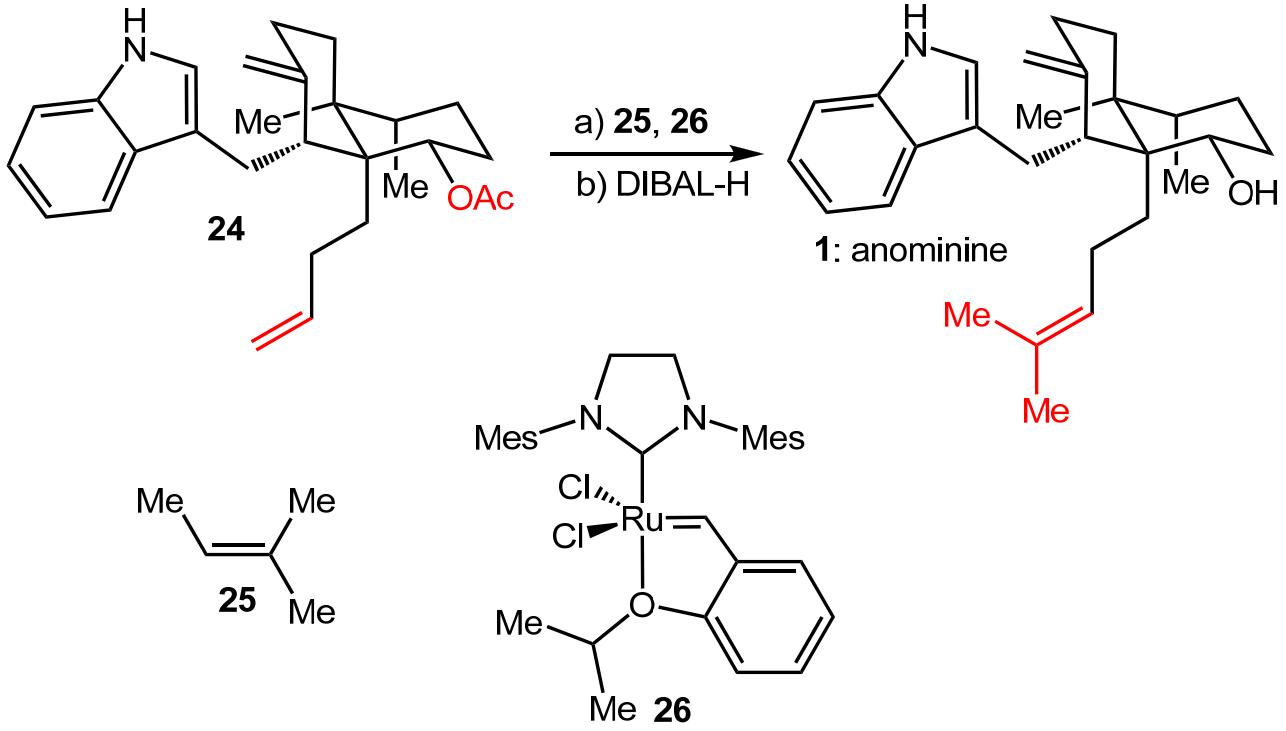
Retrosynthetic analysis of Tubingensin A (**2**)

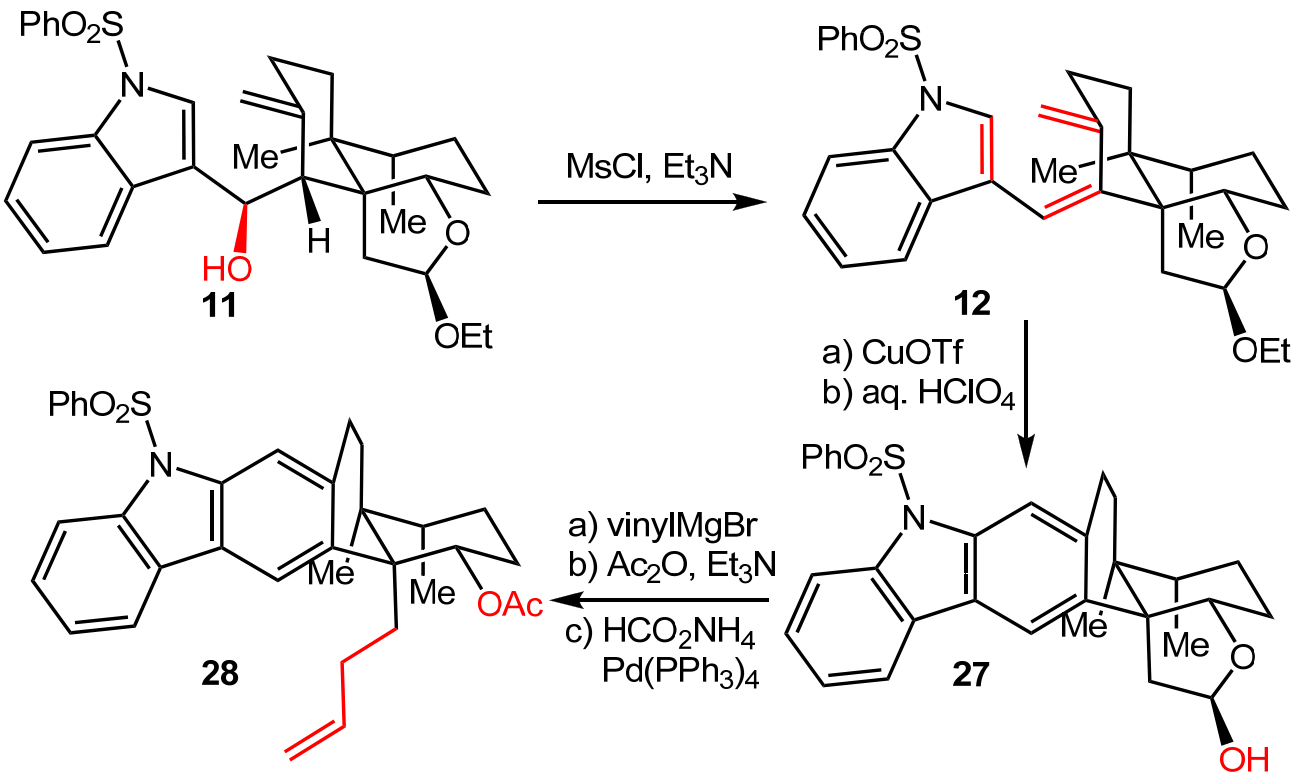


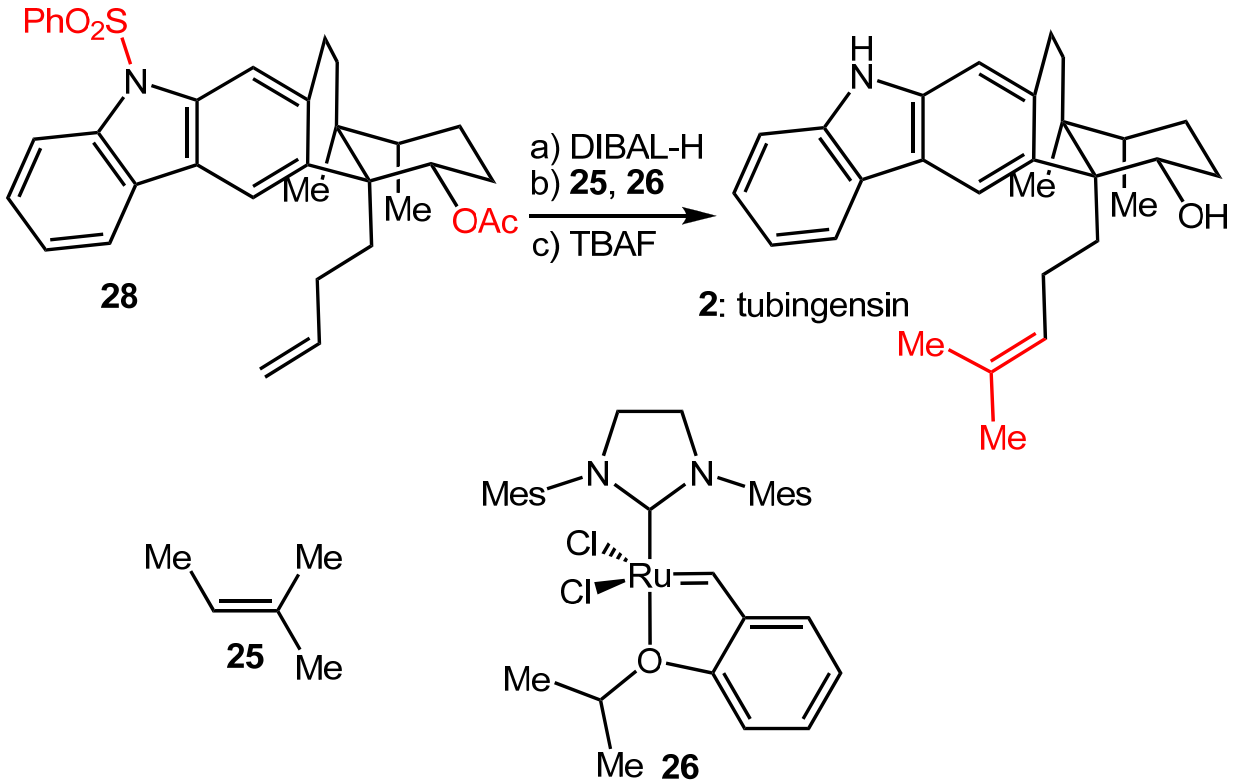

Me
Me
O
16
a) TMSCl
NaI, HMDS
b) MVK
BF3·OEt2
c) NaOMe
Me
Me
O
17
2 steps
Me
Me
O
15
OH
NIS
OEt
MVK:
O
Me
Me
Me
O
O
13
OEt
Me
Me
20
O
21
22
O
EtO
AIBN
n-Bu3SnH
HCl/EtOH
Me
Me
O
O
I
18
OEt


a) LiHMDS
TMSCl
b) HCHO
Sc(OTf)3
a) TBSCl
imidazole
b) Ph3P=CH2
c) TBAF
d) DMP
13
14
19
11
21
TsOH
PhO2S
IMg
HO
10

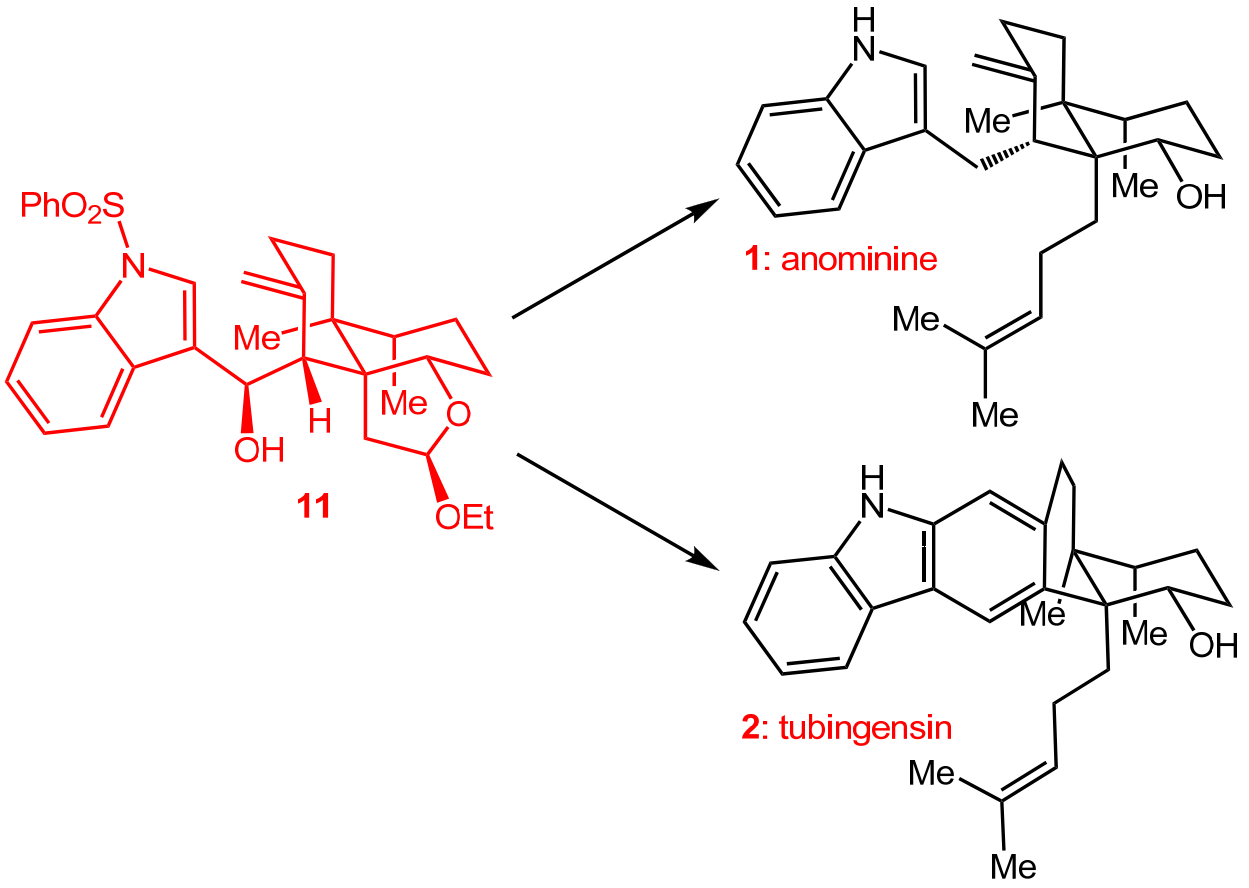

PhO2S
N
Me
HO
H
Me
O
OEt
11
a) KHMDS, CS2, MeI
b) n-Bu3SnH, AIBN
c) TBAF
H
N
Me
Me
O
OEt
22
HClO4
H
N
Me
Me
O
OH
23
a) vinylMgBr
b) Ac2O, Et3N
c) HCO2NH4
Pd(PPh3)4
H
N
Me
Me
OAc
24


H
N
Me
Me
OAc
24
a) 25, 26
b) DIBAL-H
H
N
Me
Me
OH
1: anominine
Me
Me
Me
Me
25
Mes
N
N
Mes
Cl
Cl
Ru
O
Me
Me
26


PhO2S
N
Me
H
HO
Me
O
OEt
11
MsCl, Et3N
PhO2S
N
Me
Me
O
OEt
12
a) CuOTf
b) aq. HClO4
PhO2S
N
Me
Me
O
OH
27
a) vinylMgBr
b) Ac2O, Et3N
c) HCO2NH4
Pd(PPh3)4
PhO2S
N
Me
Me
OAc
28


PhO2S
N
Mė
Me
OAc
28
a) DIBAL-H
b) 25, 26
c) TBAF
H
N
Mė
Me
OH
2: tubingensin
Me
Me
Me
Me
25
Mes
N
N
Mes
Cl
Cl
Ru
O
Me
Me
26

总结:



1, **Intermediate 11 bearing all of the required stereogenic centers.**

2, **Ueno-Stork radical cyclization.**

3, **$Sc(Otf)_3$ mediated Mukaiyama aldol reaction.**

Anominine (**1**) is a structurally representative member of a growing family of naturally occurring indole diterpenoids that also includes tubingensin A (**2**), aspernomine (**3**), aflavinine (**4**), and 10,23-dihydro-24,25-dehydroaflavinine (**5**) which were initially isolated from Aspergillus spp. by Gloer and co-workers. Several other members of this family [e.g., 17-hydroxyeujindole (**6**)] were recently isolated from Eupenicillium javanicum. Not surprisingly, these intricate molecular architectures were found to possess interesting biological properties, such as antiinsectant, antiviral, and anticancer activities. Notably, the syntheses of its congeners remain a challenge.

In conclusion, we have described efficient total syntheses of anominine and tubingensin A, the latter of which has been accomplished for the first time. A divergent strategy based on a versatile common intermediate **11** was successfully applied in our syntheses. A series of reactivity and selectivity problems were encountered and overcome on the journey. These studies are expected to facilitate the systematic synthetic and biological investigations of the members of this indole terpenoid family. These ongoing studies should further corroborate the biosynthetic speculations on this family of natural products.