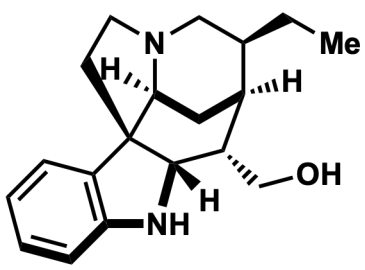
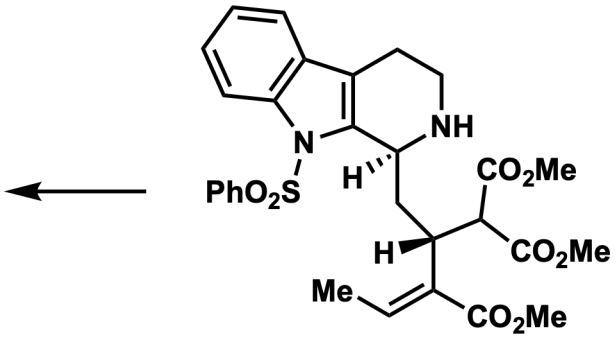
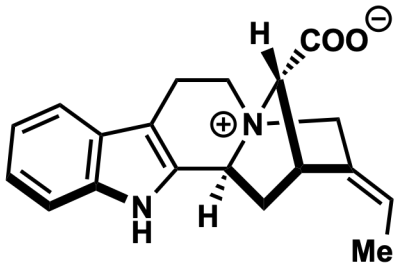
Divergent Total Synthesis of 17-nor-Excelsinidine and Geissoschizoline



Geissoschizoline



Common Intermediate



17-nor-Excelsinidine

Courtney D. Glenn
ChemSyn Presentation
October 08, 2026

Corresponding Author Highlight

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Divergent Total Synthesis of 17-*nor*-Excelsinidine and Geissoschizoline

Zhi-Qi Cao, Ya-Kui Sun, Hui Shao,* and Yu-Ming Zhao*

Cite This: *Org. Lett.* 2026, 28, 11720–11725 Read Online



PhD., Lanzhou University, (2005-10)
Lecturer, Lanzhou University, (2010-11)
Postdoc, The Hong Kong University of Science and Technology, (2011-12)
Postdoc (Maimone Group), UC Berkeley, (2012-14)
Principal Investigator, Shaanxi Normal University (From 2015-present)

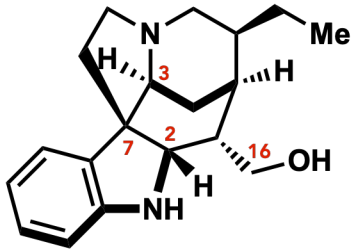
Prof. Yu-Ming Zhao



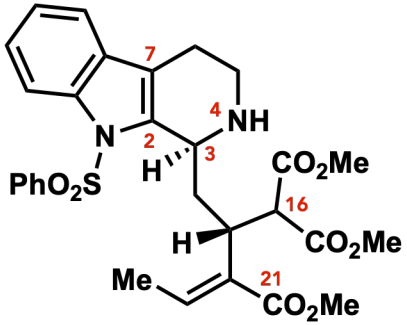
PhD., Lanzhou University, (2016)
Postdoc, Shanghai Jiao Tong University (2016–2019)
Postdoc (Zhao Group), Shaanxi Normal University (2019–2022)
Principal Investigator, Shaanxi Normal University (From 2023-present)

Prof. Hui Shao

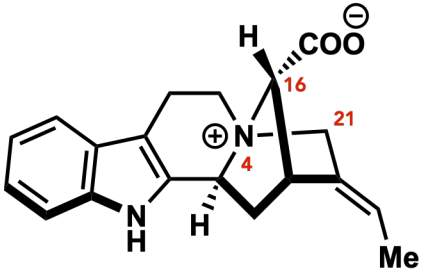
Background



Geissoschizoline



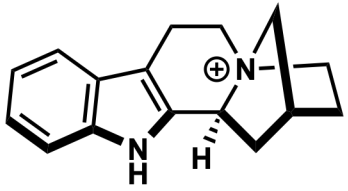
Common Intermediate



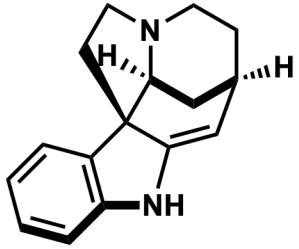
17-nor-Excelsinidine

Plant Secondary Metabolites

monoterpenoid indole alkaloids



Excelsinidine skeleton



Strychnos skeleton



Alstonia species of the Apocynaceae family



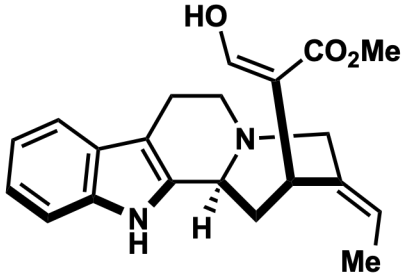
Strychnos species of the Loganiaceae family

Strychnos Alkaloids (Geissoschizoline)

– pentacyclic [6.5.6.6.5] skeleton
– aza-[3,3,1] bridged ring unit
– Anti-flammatory activity and potential treatement for Alzheimer's disease

Excelsinidine Alkaloids (17-nor-Excelsinidine)

– pentacyclic [6.5.6.5.5] skeleton
– aza-[2.2.1] bridged ring unit
– inhibitory activity again herpes simplex virus (HSV) and adenovirus (ADV)

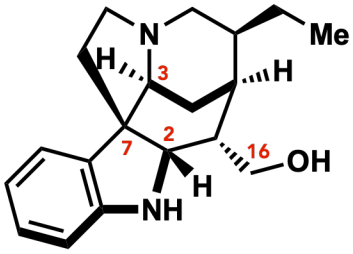


19*E*-Geissoschizine

Biosynthetic precursor to *17-nor-Excelsinidine* and *Geissoschizoline*

references: *JACS Au* **2025**,*5*,4956−4962; *Org. Lett.* **2026**, *28*, 11720−11725

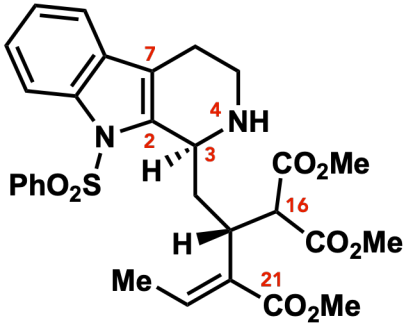
Divergent Total Synthesis of 17-nor-Excelsinidine and Geissoschizoline



Geissoschizoline

Biomimetic synthesis

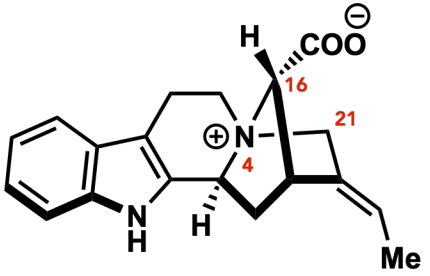
7 steps



Common Intermediate

Oxidative cyclization & Intramolecular N-alkylation

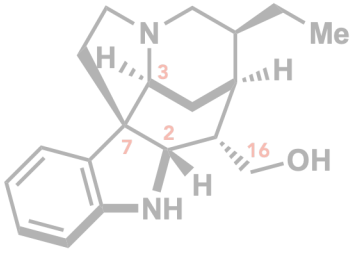
7 steps



17-nor-Excelsinidine

references: *JACS Au* **2025**,*5*,4956−4962; *Org. Lett.* **2026**, *28*, 11720−11725

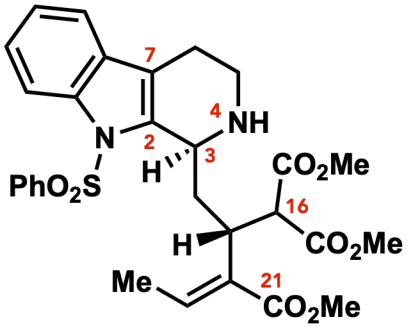
Divergent Total Synthesis of 17-nor-Excelsinidine and Geissoschizoline



Geissoschizoline

Biomimetic synthesis

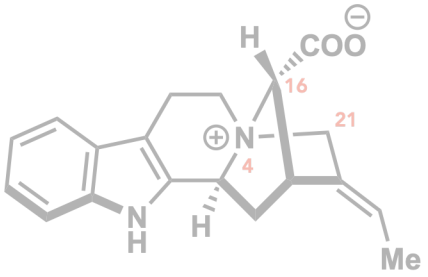
7 steps



Common Intermediate

Oxidative cyclization & Intramolecular N-alkylation

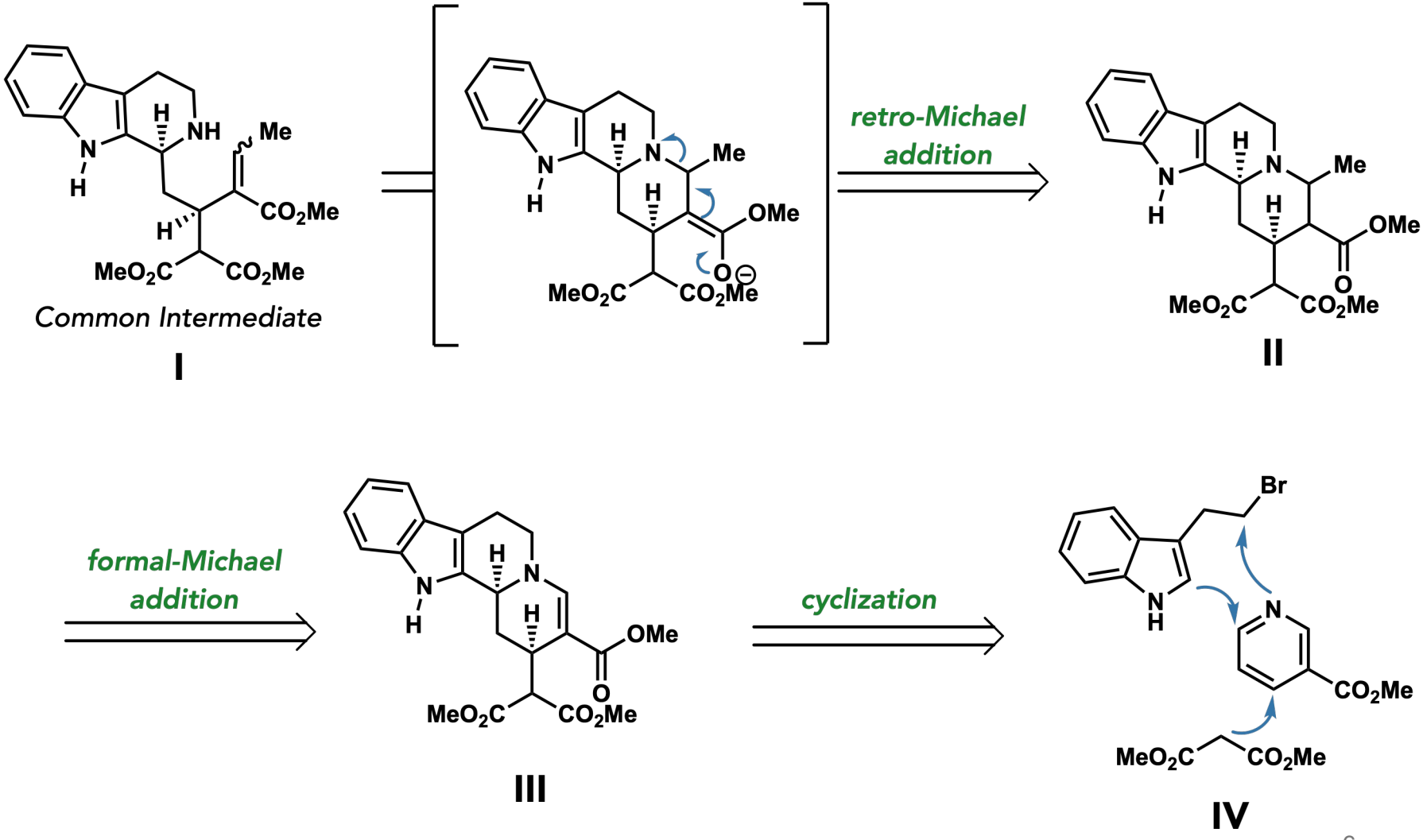
7 steps



17-nor-Excelsinidine

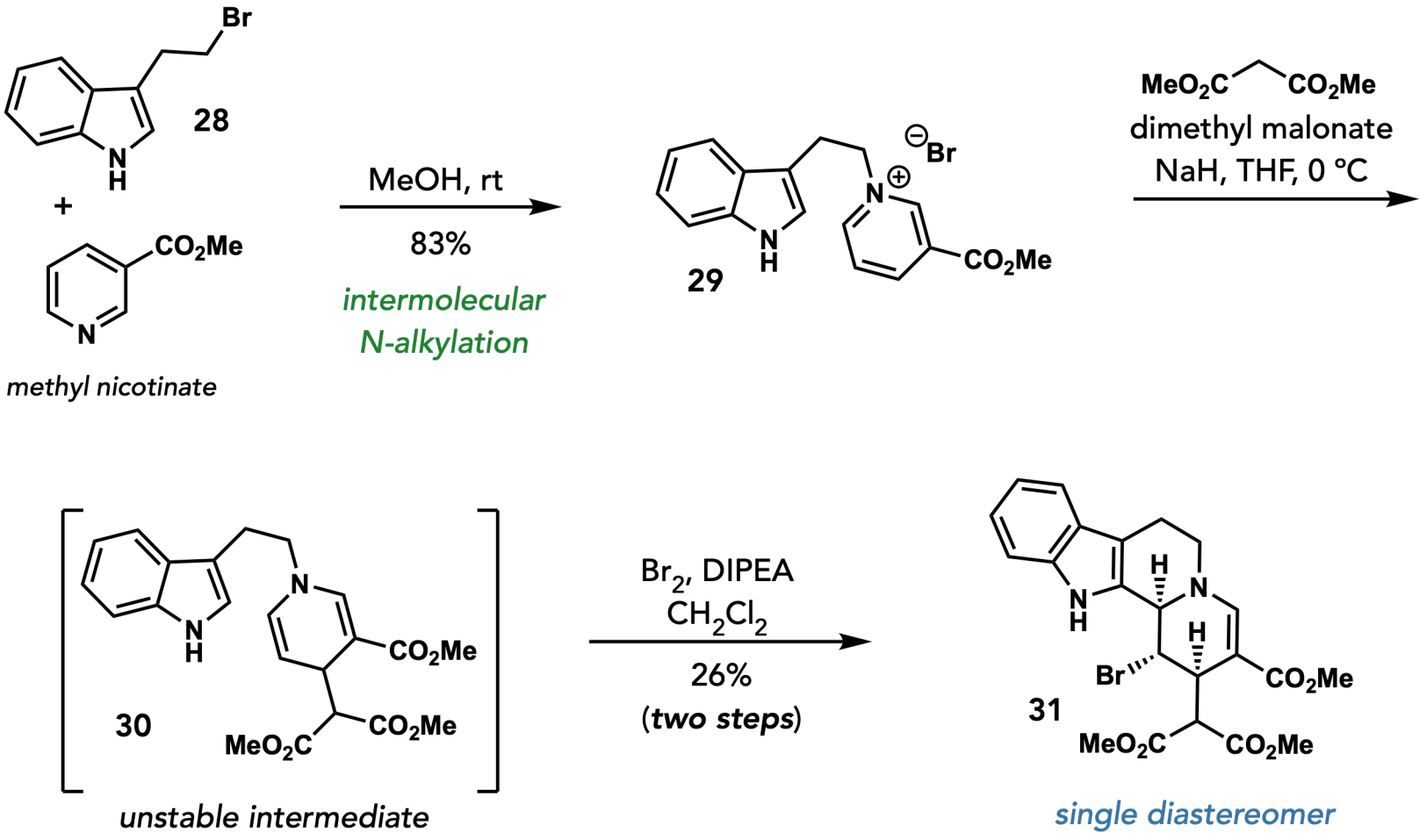
references: *JACS Au* **2025**,*5*,4956−4962; *Org. Lett.* **2026**, *28*, 11720−11725

Retrosynthetic Pathway to Common Intermediate



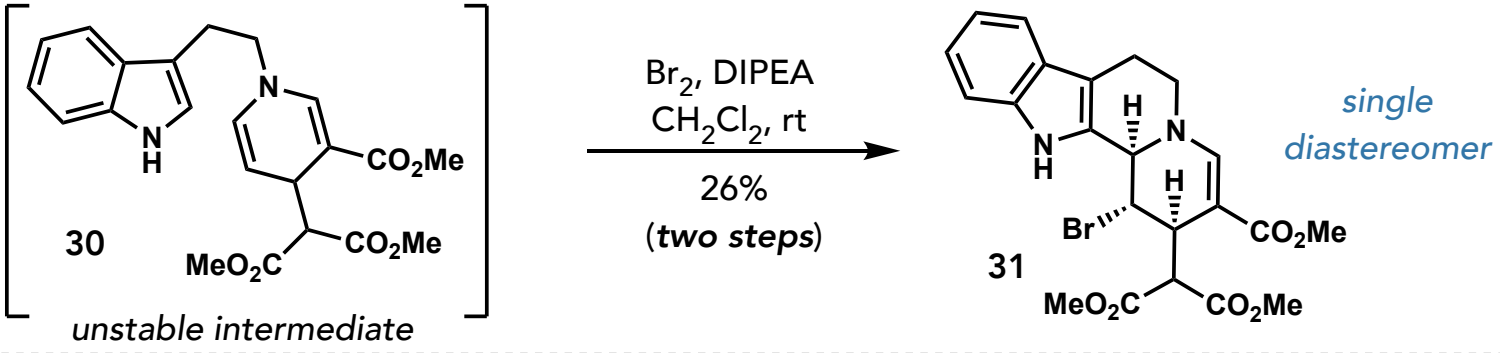
references: *JACS Au* **2025**,*5*,4956−4962

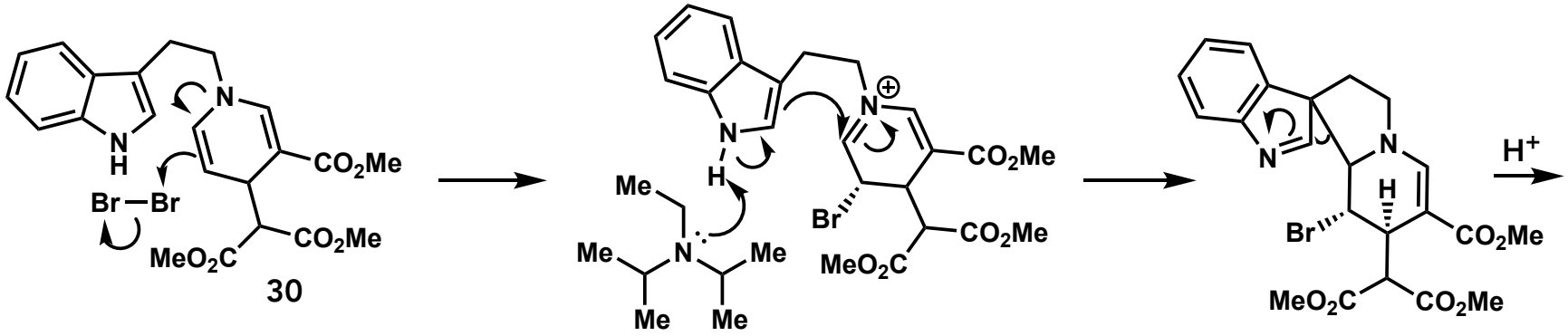
Synthetic Route to Common Intermediate

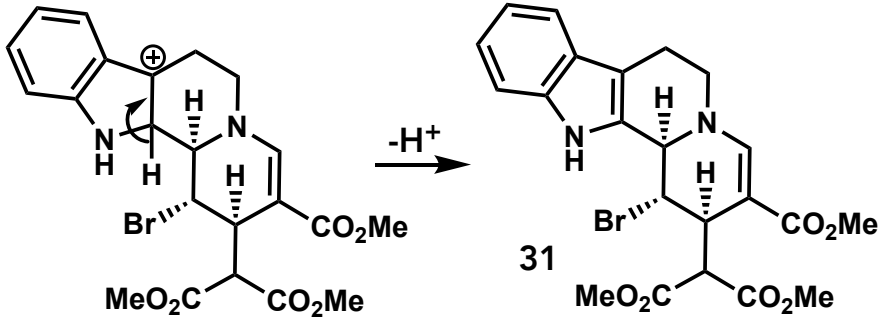


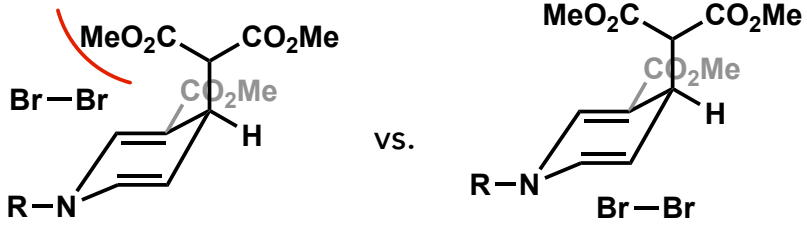
references: *JACS Au* **2025**,*5*,4956−4962

Mechanism 30 to 31

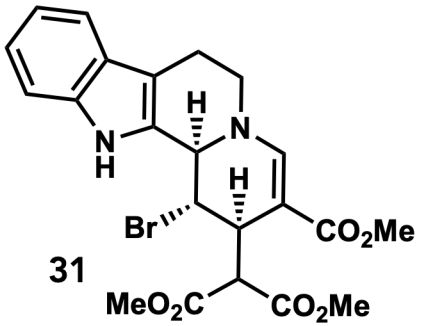








Synthetic Route to Common Intermediate



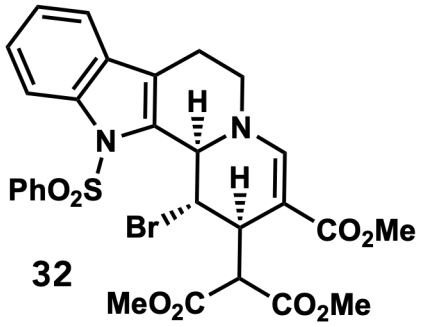
31

single diastereomer

NaOH, $PhSO_2Cl$,
DMAP, CH_2Cl_2, rt

87%

indole sulfonyl protection

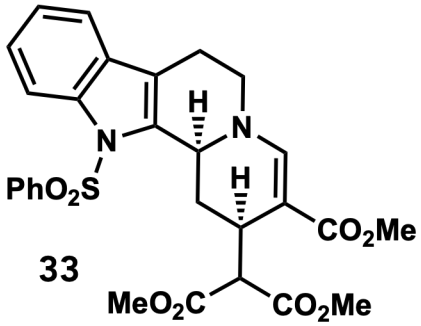


32

$^nBu_3SnH$, AIBN,
PhH, 80 °C

85%

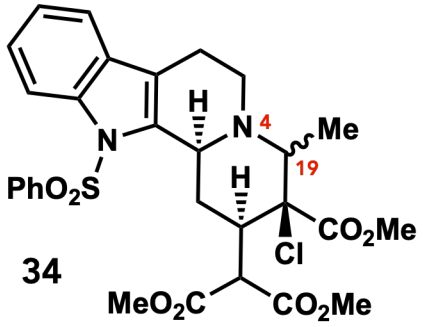
radical mediated dehalogenation



33

NCS, CH_2Cl_2, 0 °C
then $AlMe_3$

84%
(dr = 5:3)

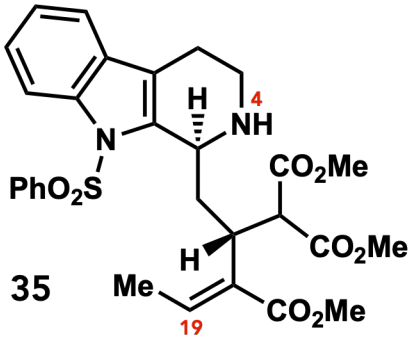


34

TMSCl, $ZnCl_2$, Zn, THF
rt-40 °C

85%

retro-aza Michael addition

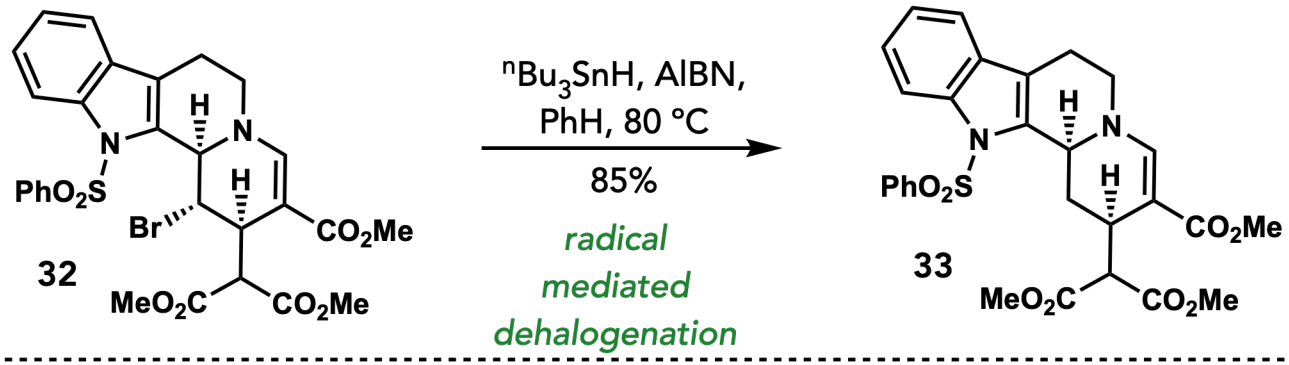


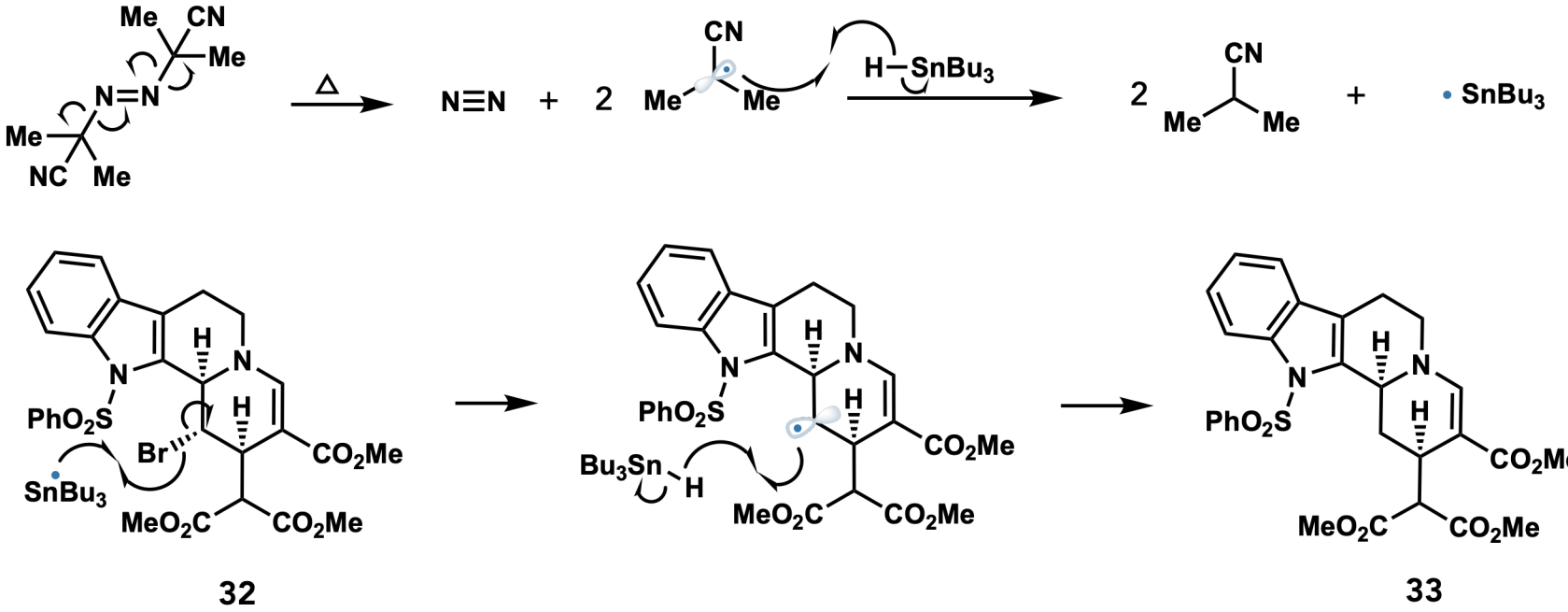
35

Common Intermediate
single diastereomer

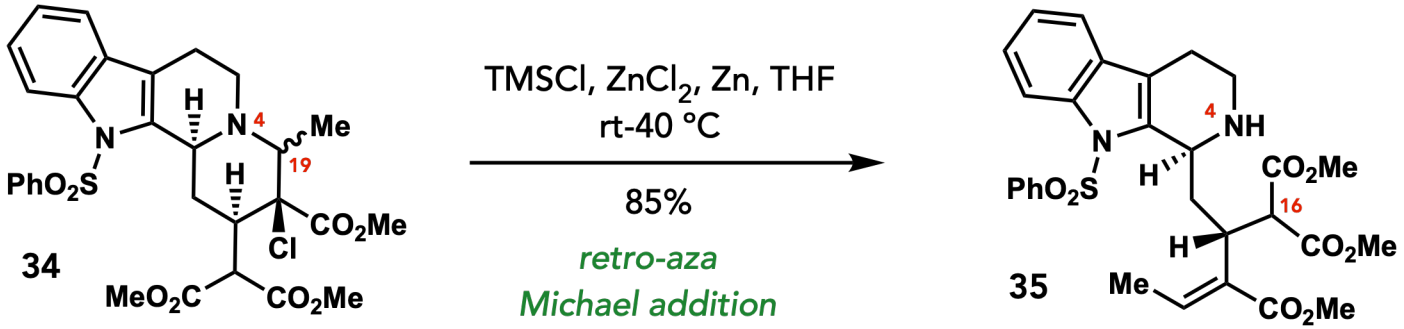
references: *JACS Au* **2025**,*5*,4956−4962

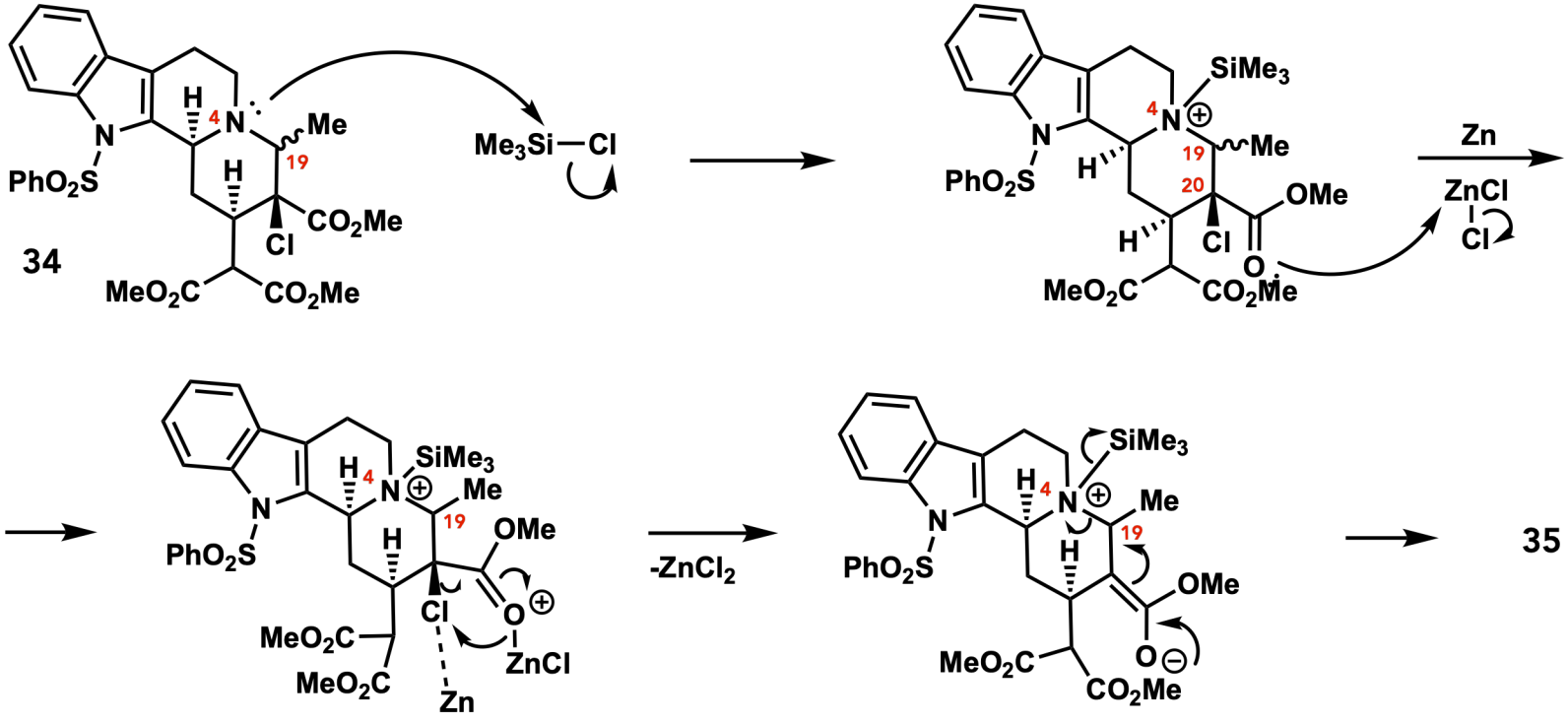
Mechanism 32 to 33



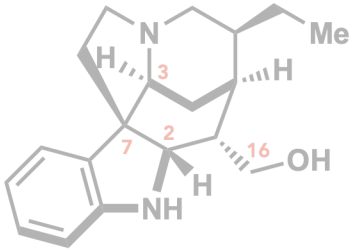


Mechanism 34 to 35





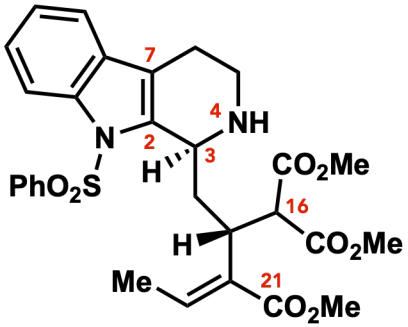
Divergent Total Synthesis of 17-nor-Excelsinidine and Geissoschizoline



Geissoschizoline

Biomimetic synthesis

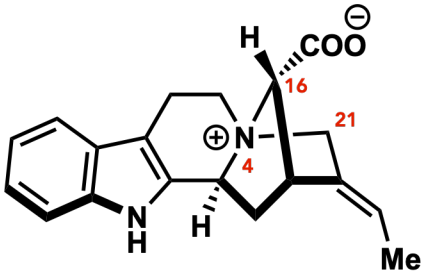
7 steps



Common Intermediate

Oxidative cyclization & Intramolecular N-alkylation

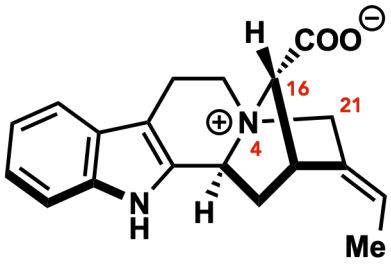
7 steps



17-nor-Excelsinidine

references: *Org. Lett.* **2026**, *28*, 11720−11725

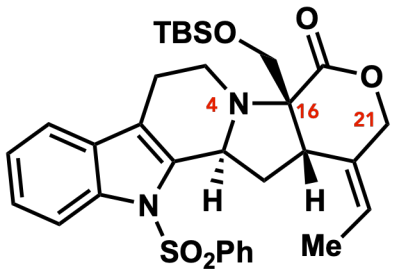
Retrosynthetic Pathway to 17-nor-Excelsinidine



17-nor-Excelsinidine

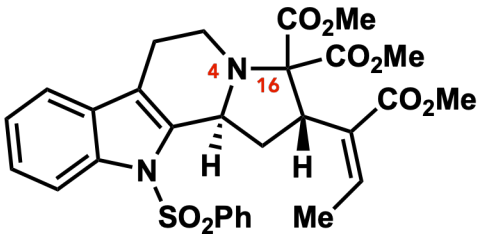
I

Intramolecular N-alkylation



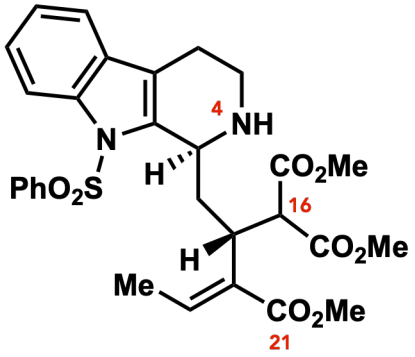
II

FGI



III

Oxidative cyclization

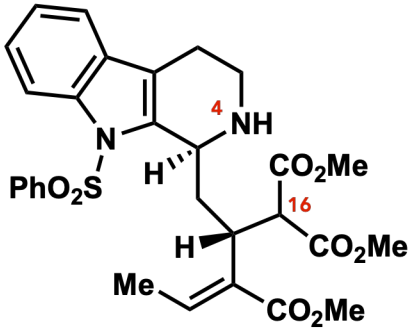


Common Intermediate

IV

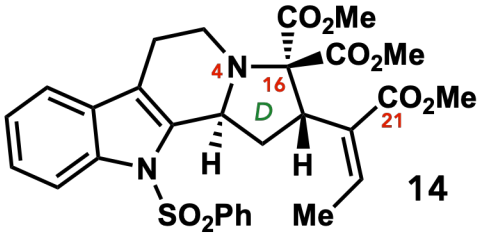
references: *Org. Lett.* **2026**, *28*, 11720−11725

Synthetic Pathway to 17-nor-Excelsinidine



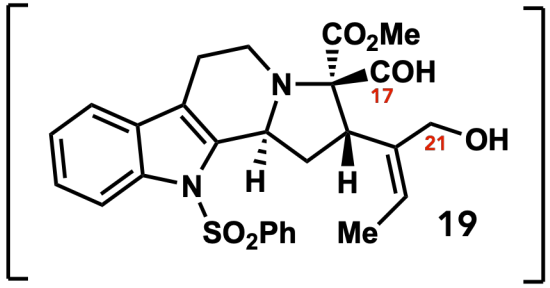
Common Intermediate

NBS
then DBU, DCE
72%



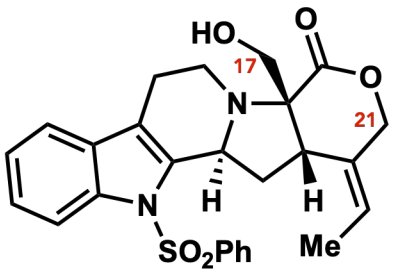
14

DIBAL–H
CH_2Cl_2

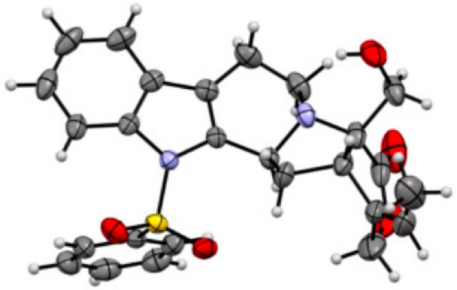


19

then $NaBH_4$
MeOH
70%

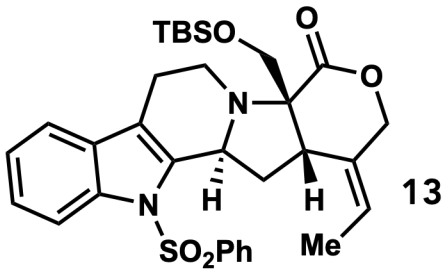


20



20 [X-ray]
(CCDC 2579442)

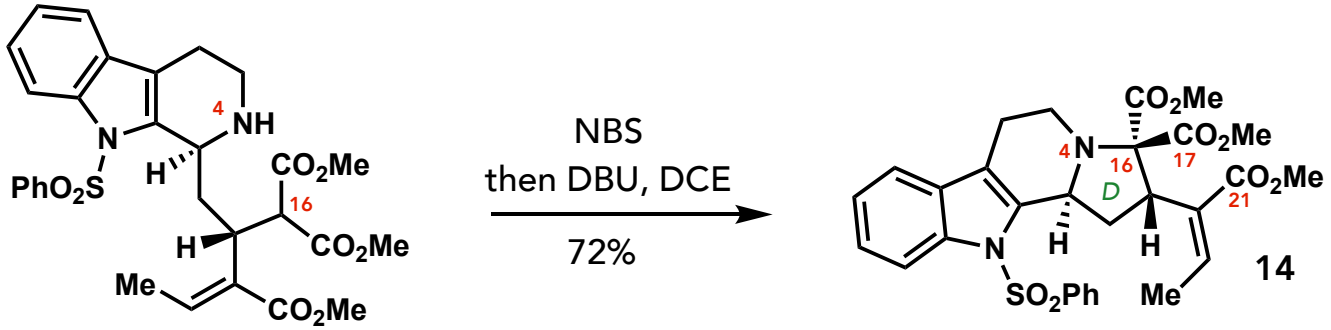
TBSCl
imidazole, CH_2Cl_2
76%

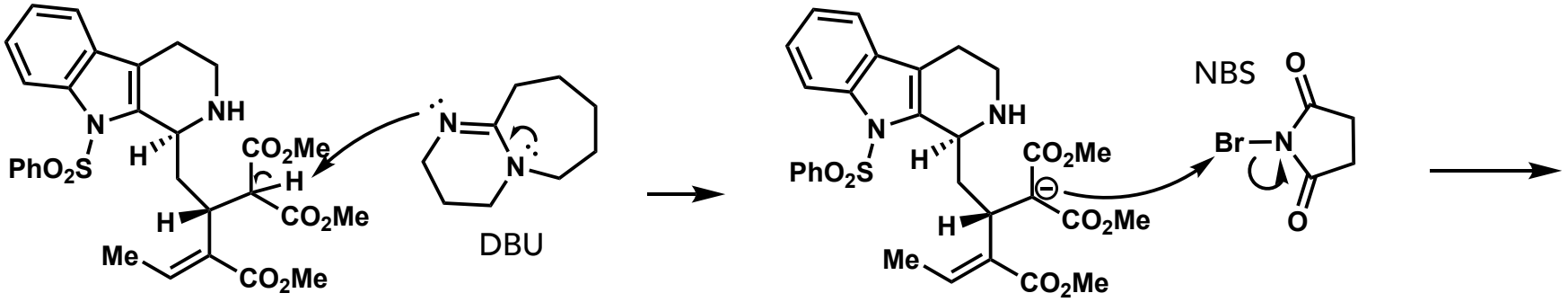


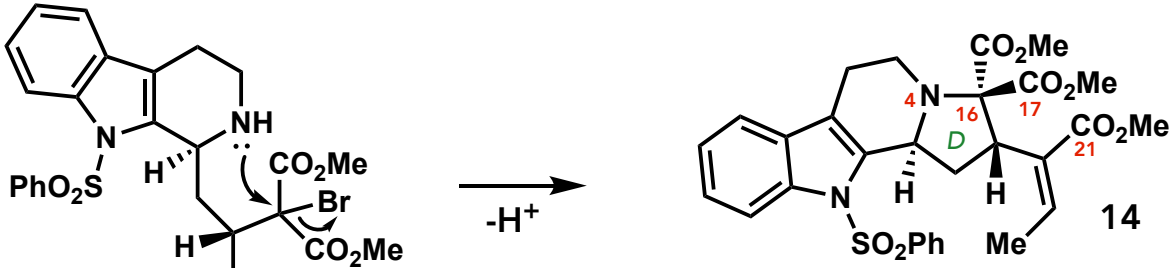
13

references: *Org. Lett.* **2026**, *28*, 11720–11725

Mechanism Common Intermediate to 14

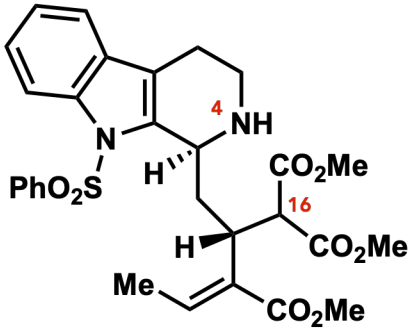






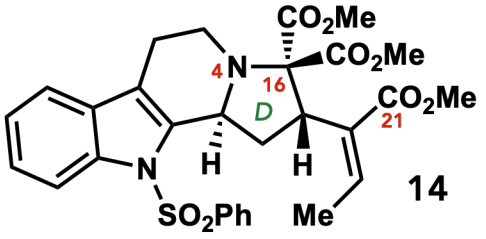
Rigid tetracyclic framework fixes the orientation of the esters

Synthetic Pathway to 17-nor-Excelsinidine



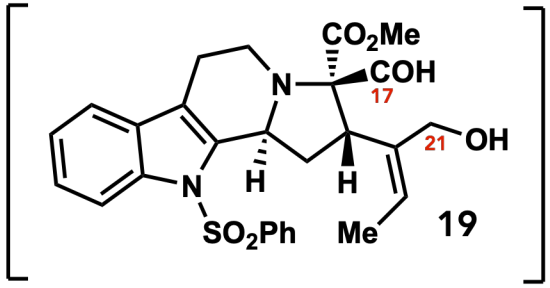
Common Intermediate

NBS
then DBU, DCE
72%



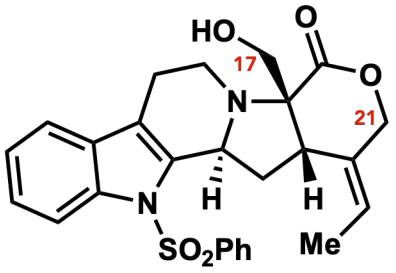
14

DIBAL–H
CH_2Cl_2

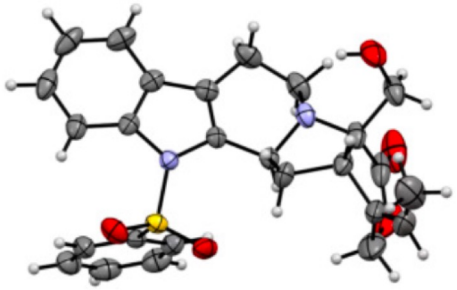


19

then $NaBH_4$
MeOH
70%

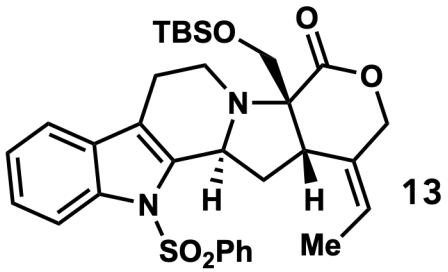


20



20 [X-ray]
(CCDC 2579442)

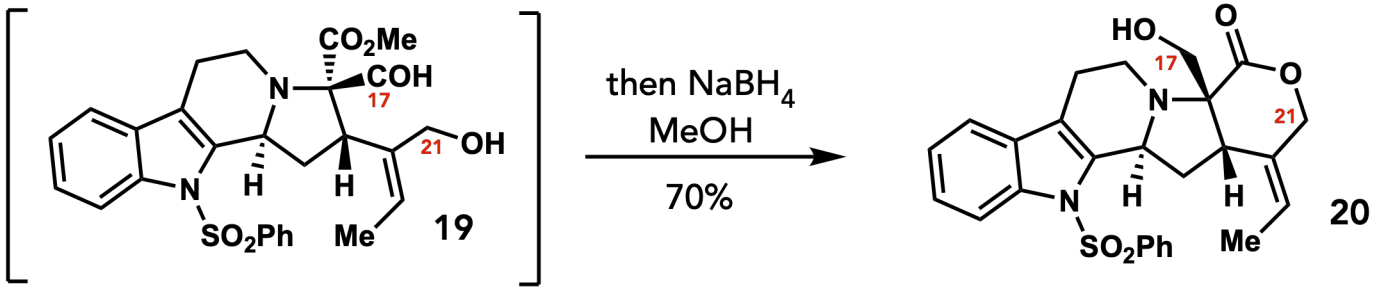
TBSCl
imidazole, CH_2Cl_2
76%

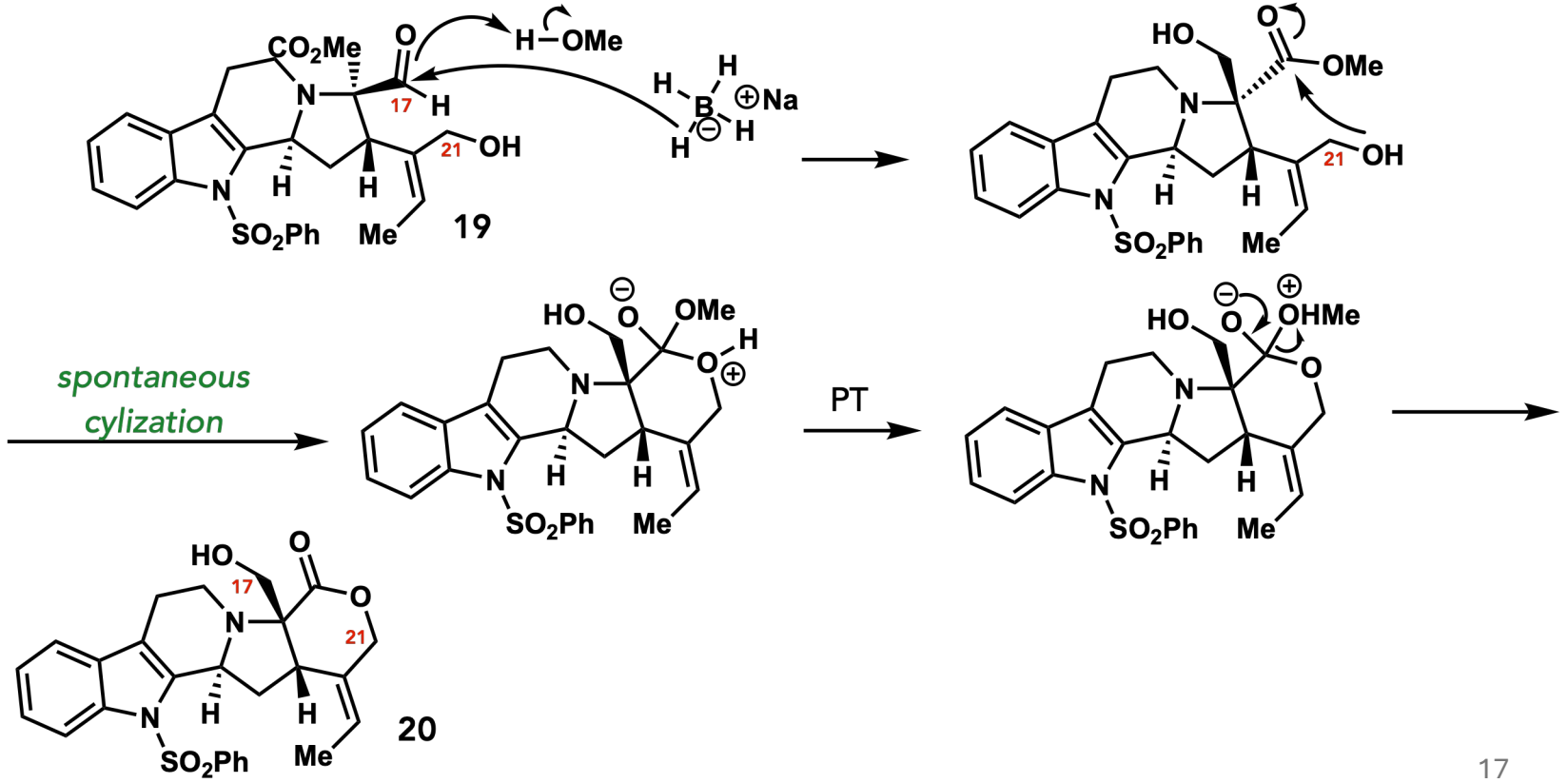


13

references: *Org. Lett.* **2026**, *28*, 11720–11725

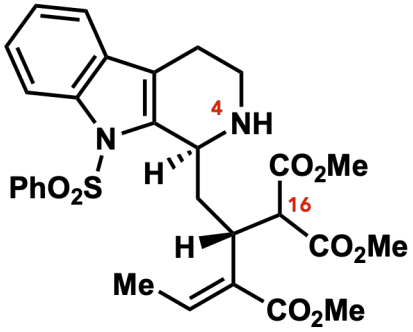
Mechanism 19 to 20





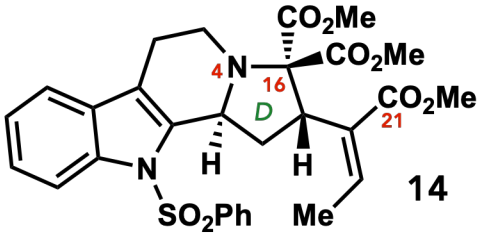
references: *Org. Lett.* **2026**, *28*, 11720–11725

Synthetic Pathway to 17-nor-Excelsinidine



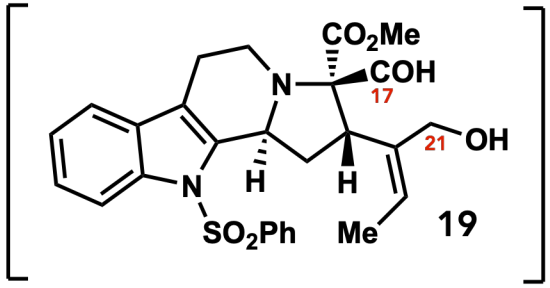
Common Intermediate

NBS
then DBU, DCE
72%



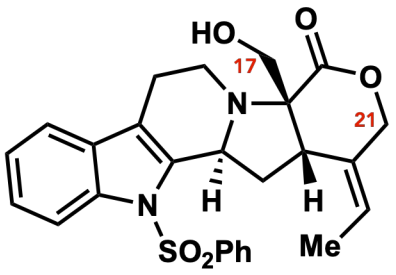
14

DIBAL–H
CH_2Cl_2

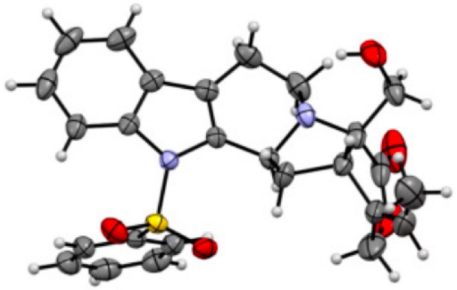


19

then $NaBH_4$
MeOH
70%

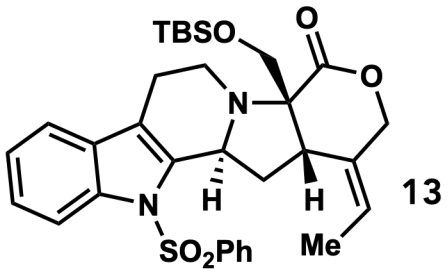


20



20 [X-ray]
(CCDC 2579442)

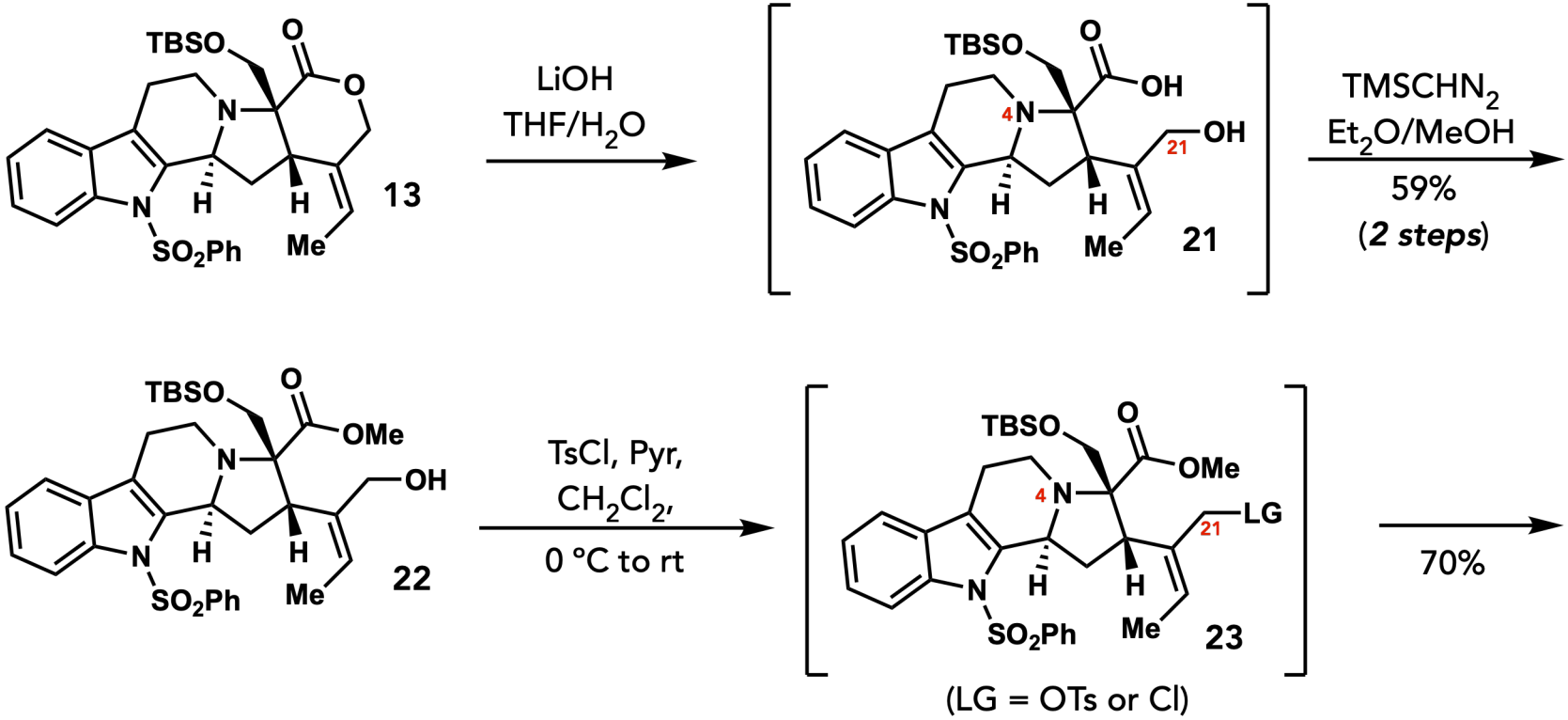
TBSCl
imidazole, CH_2Cl_2
76%



13

references: *Org. Lett.* **2026**, *28*, 11720–11725

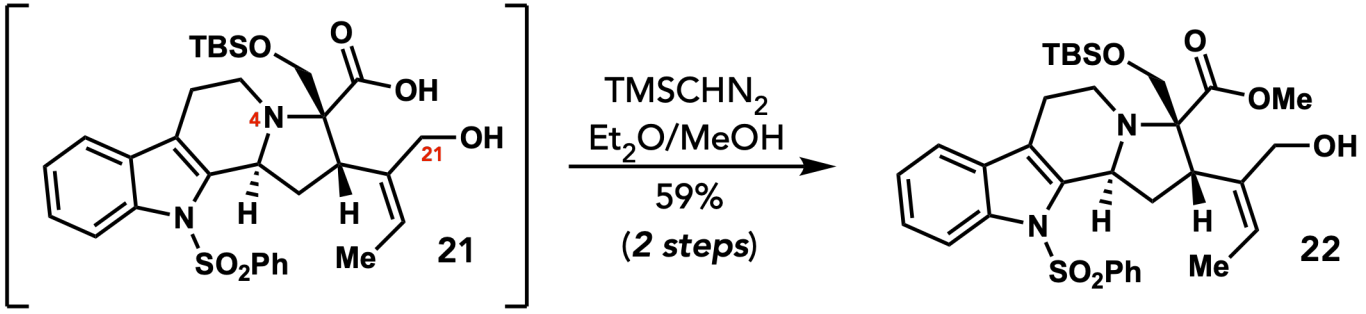
Synthetic Pathway to 17-nor-Excelsinidine

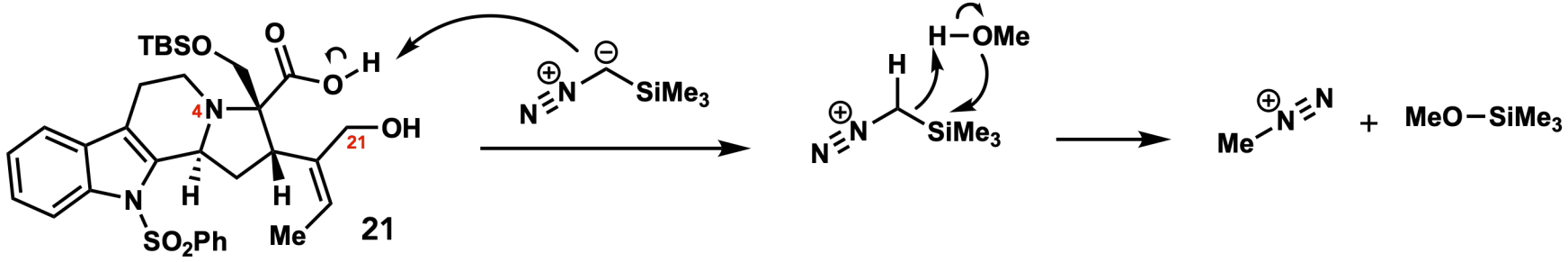


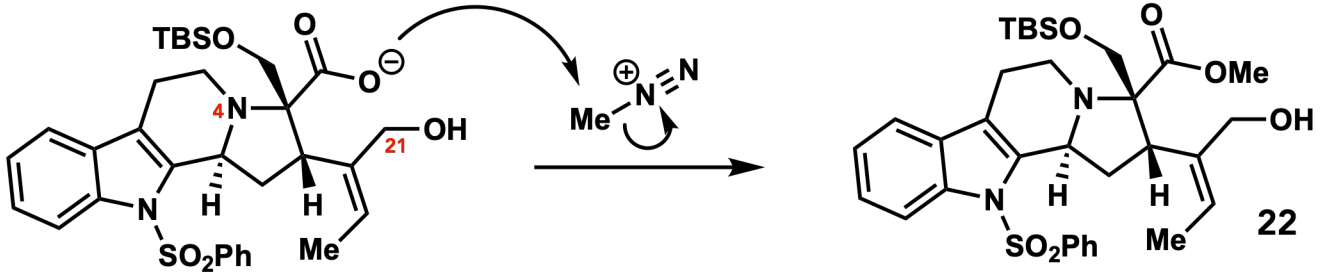
CsF-promoted desilylation
retro-aldol reaction
benzenesulfonyl deprotection
methyl ester hydrolysis

references: *Org. Lett.* **2026**, *28*, 11720–11725

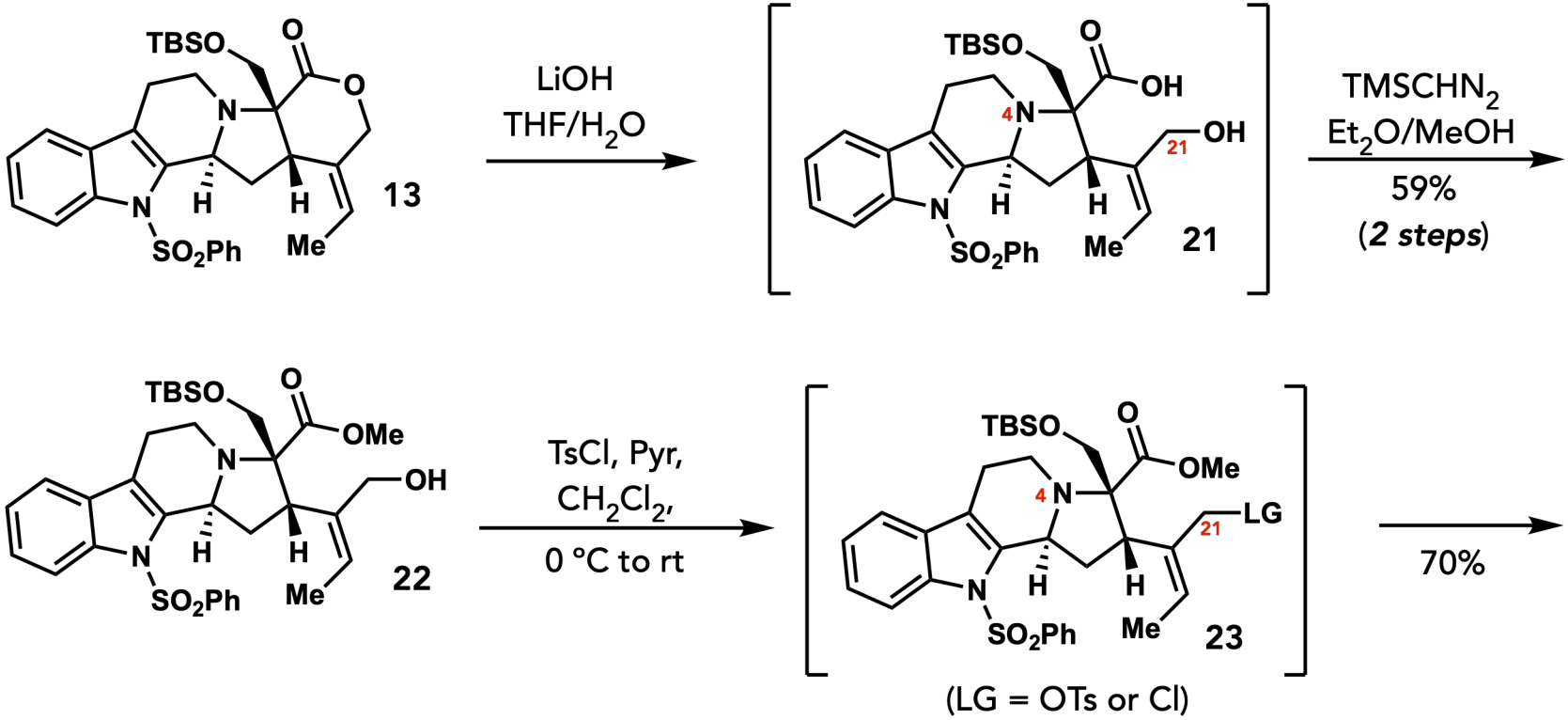
Mechanism 21 to 22







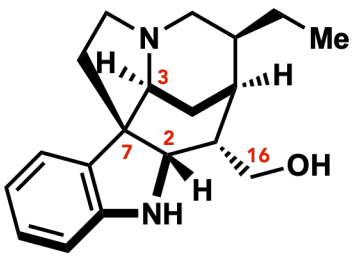
Synthetic Pathway to 17-nor-Excelsinidine



CsF-promoted desilylation
retro-aldol reaction
benzenesulfonyl deprotection
methyl ester hydrolysis

references: *Org. Lett.* **2026**, *28*, 11720–11725

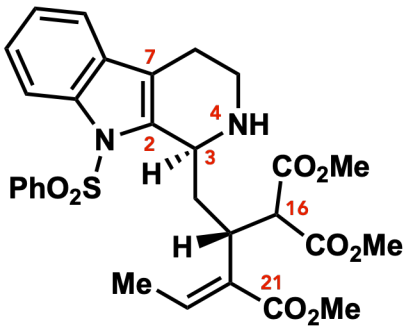
Divergent Total Synthesis of 17-nor-Excelsinidine and Geissoschizoline



Geissoschizoline

Biomimetic synthesis

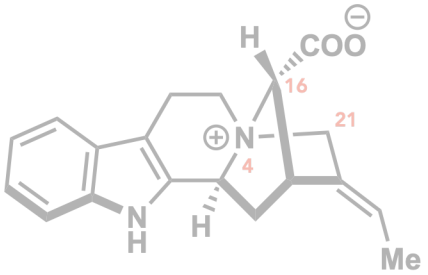
7 steps



Common Intermediate

Oxidative cyclization & Intramolecular N-alkylation

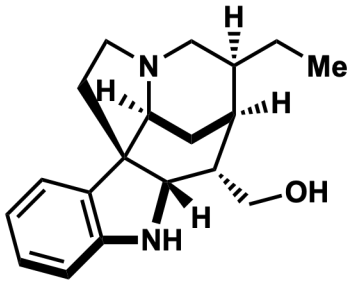
7 steps



17-nor-Excelsinidine

references: *Org. Lett.* **2026**, *28*, 11720–11725

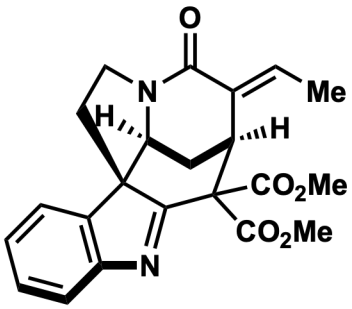
Retrosynthetic Route to Geissoschizoline



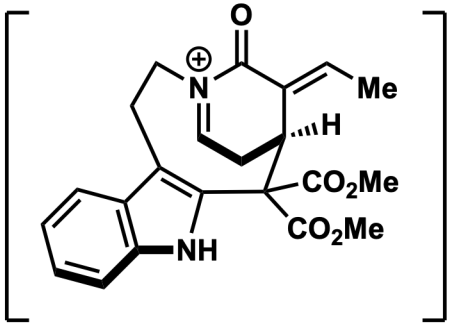
Geissoschizoline

I

Redox



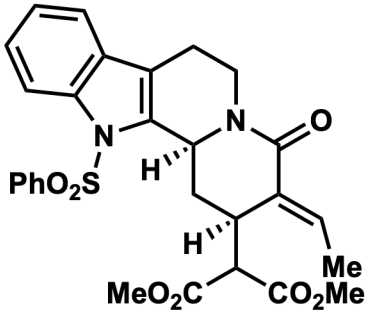
II



III

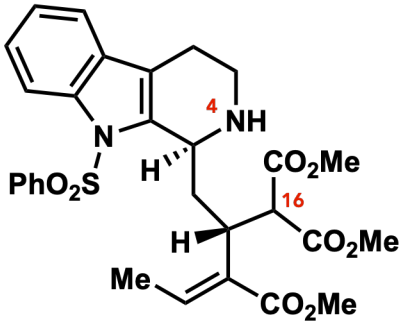
Oxidative cyclization

Skeleton reorganization



IV

Lactamization

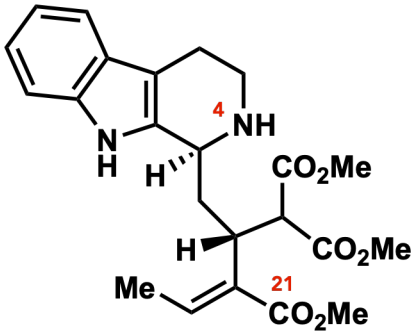


Common Intermediate

V

references: *Org. Lett.* **2026**, *28*, 11720–11725

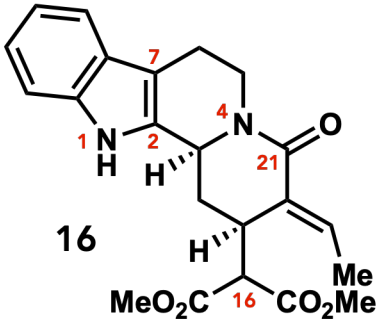
Synthetic Route to Geissoschizoline



Common Intermediate

1) LiHMDS, THF, 84%

2) Mg, MeOH, 90%

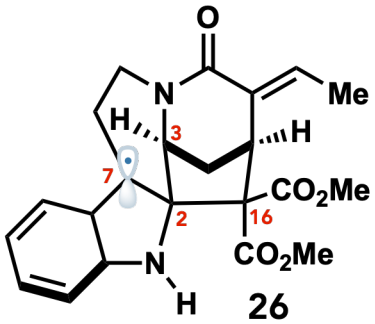


16

$Mn(OAc)_3 \bullet 2H_2O$

EtOH, 82%

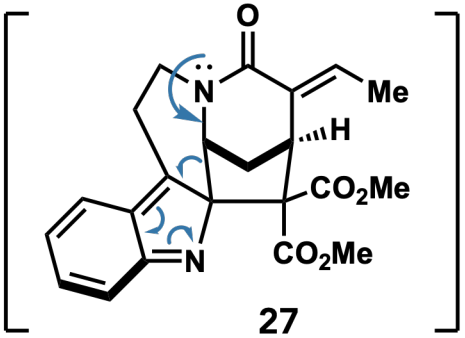
oxidative cyclization



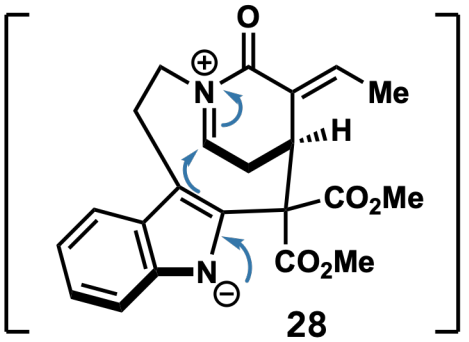
26

[O]

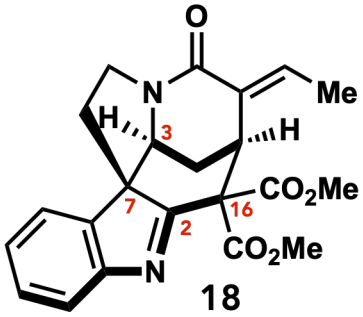
$-H^+$



27

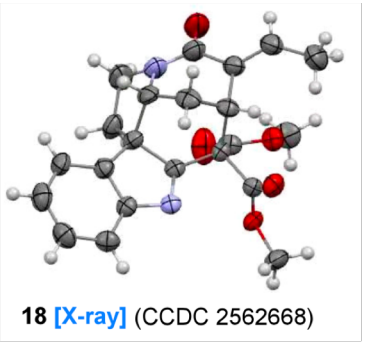


28



18

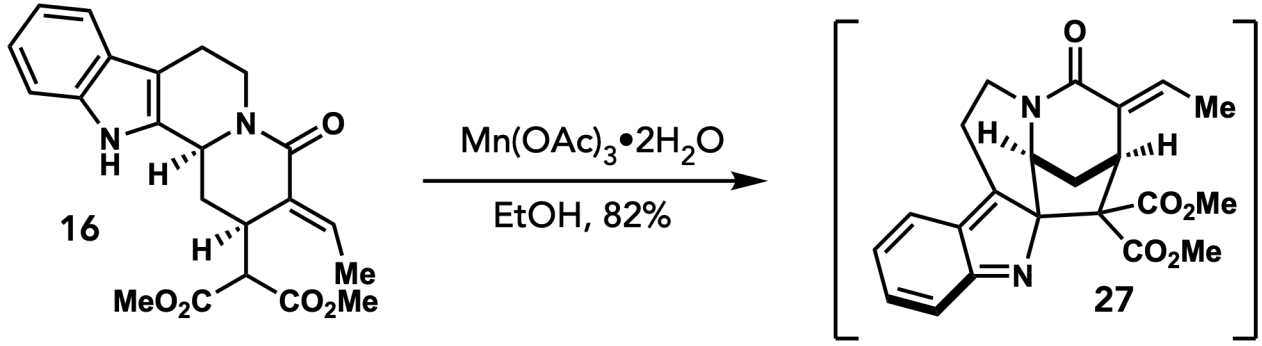
≡

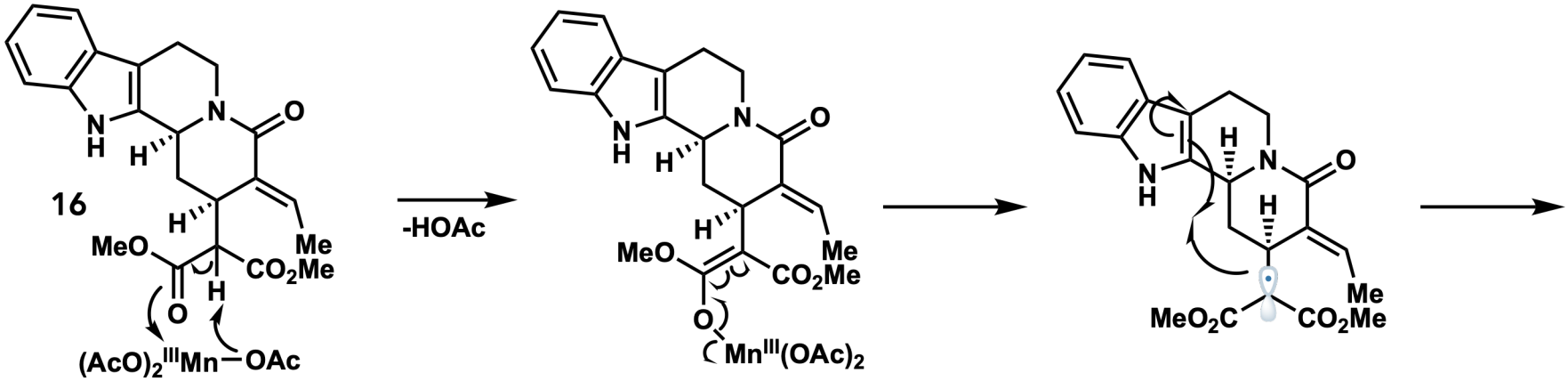


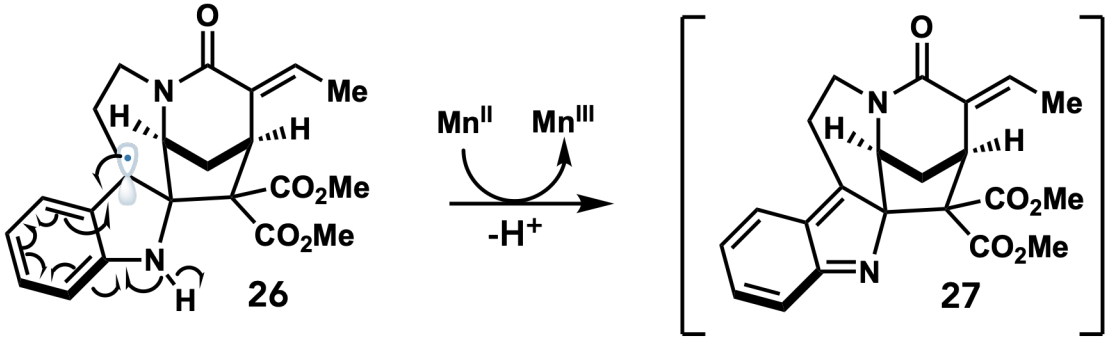
18 [X-ray] (CCDC 2562668)

references: *Org. Lett.* **2026**, *28*, 11720–11725

Mechanism 16 to 27







dearomatized species

Synthetic Route to Geissoschizoline

Common Intermediate

1) LiHMDS, THF, 84%

2) Mg, MeOH, 90%

16

$Mn(OAc)_3 \bullet 2H_2O$

EtOH, 82%

oxidative cyclization

[O]

$-H^+$

26

27

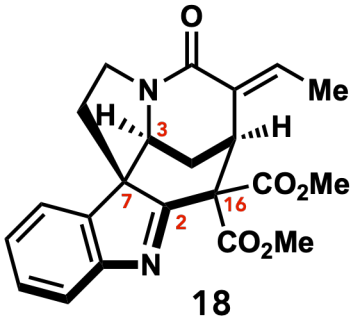
28

18

18 [X-ray] (CCDC 2562668)

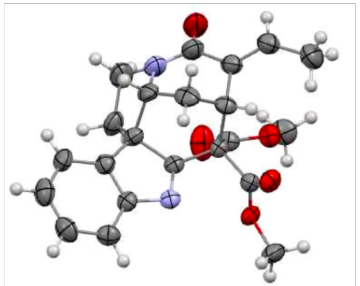
references: *Org. Lett.* **2026**, *28*, 11720–11725

Synthetic Route to Geissoschizoline



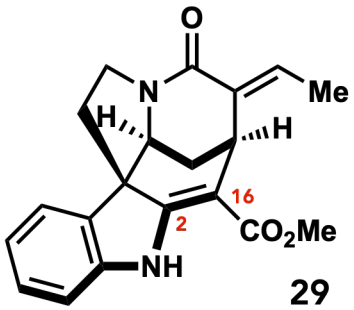
18

≡



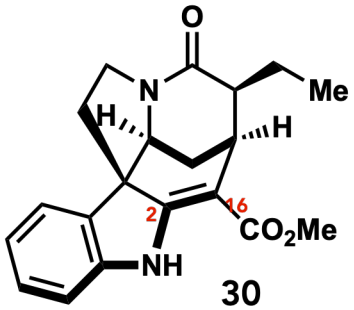
18 [X-ray] (CCDC 2562668)

$\xrightarrow[\text{DMSO/H}_2\text{O}]{\text{LiCl}}$
microwave, 78%
Krapcho decarboxylation



29

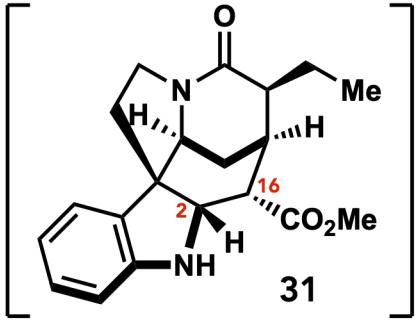
$\xrightarrow[\text{THF, 88\%}]{\text{BH}_3\bullet\text{Me}_2\text{S}}$



30

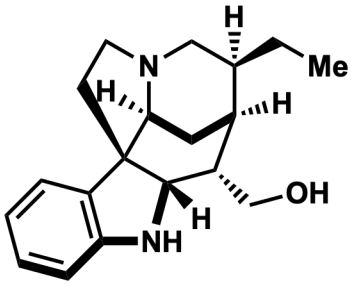
single diastereomer

$\xrightarrow[\text{NaBH}_3\text{CN}]{\text{AcOH}}$



31

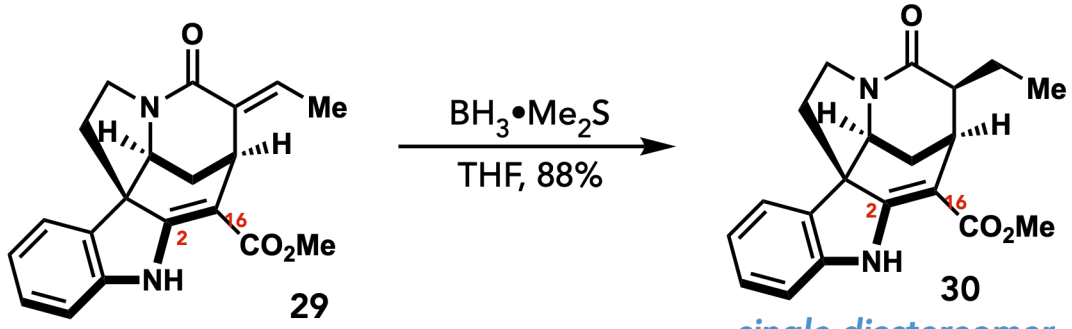
$\xrightarrow[\text{PhMe, 130 °C}]{\text{Red-Al}}$
75%
(*two steps*)

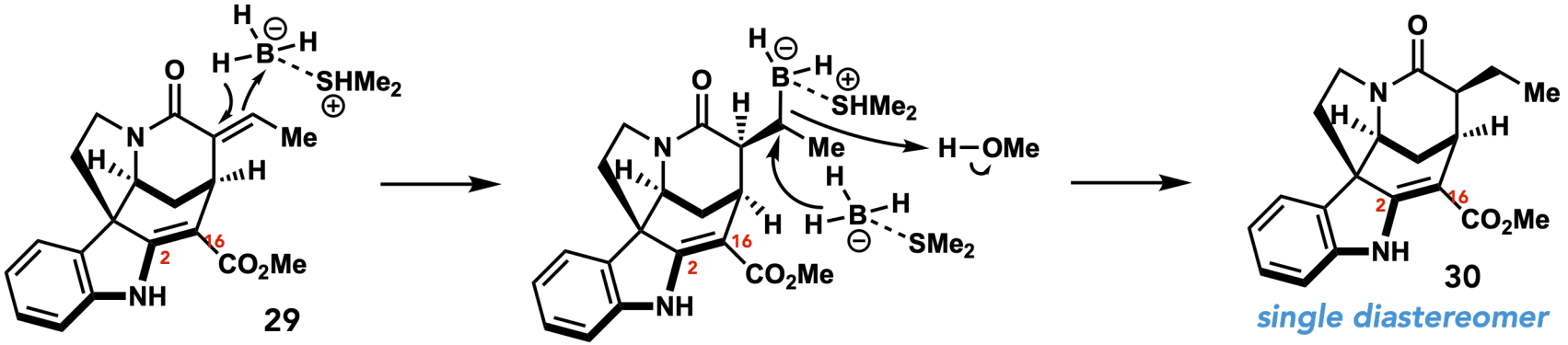


Geissoschizoline

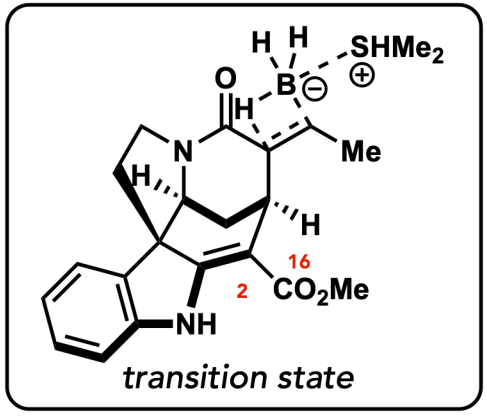
references: *Org. Lett.* **2026**, *28*, 11720–11725; 10k) *Angew. Chem. Int. Ed.* **2015**, *54*, 12632 –12635.

Mechanism 29 to 30

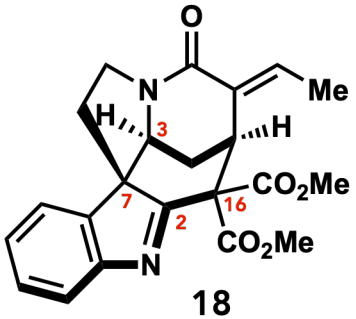




syn addition less hindered back face

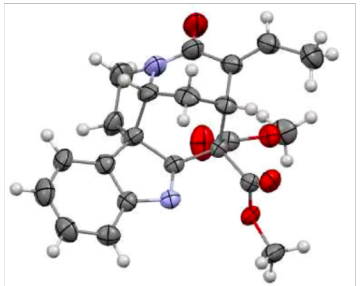


Synthetic Route to Geissoschizoline



18

≡



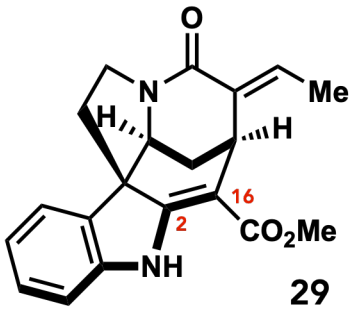
18 [X-ray] (CCDC 2562668)

LiCl

$DMSO/H_2O$

microwave, 78%

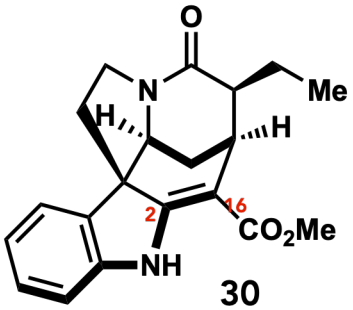
Krapcho decarboxylation



29

$BH_3 \bullet Me_2S$

THF, 88%

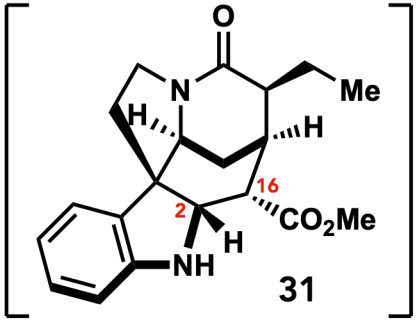


30

single diastereomer

AcOH

$NaBH_3CN$



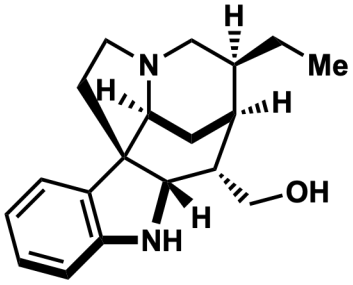
31

Red-Al

PhMe, 130 °C

75%

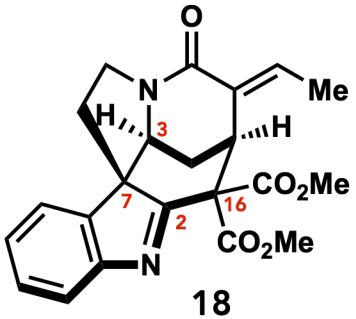
(***two steps***)



Geissoschizoline

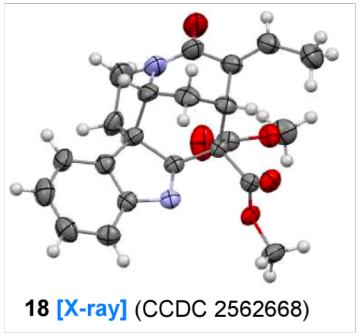
references: *Org. Lett.* **2026**, *28*, 11720–11725; 10k) *Angew. Chem. Int. Ed.* **2015**, *54*, 12632 –12635.

Synthetic Route to Geissoschizoline



18

≡



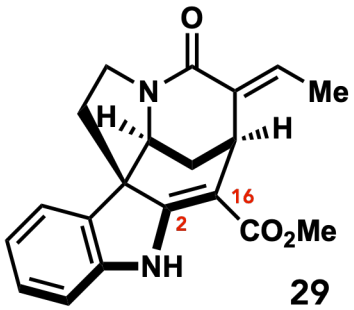
18 [X-ray] (CCDC 2562668)

LiCl

DMSO/H_2O

microwave, 78%

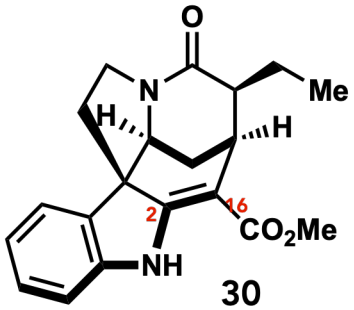
Krapcho decarboxylation



29

$BH_3 \bullet Me_2S$

THF, 88%

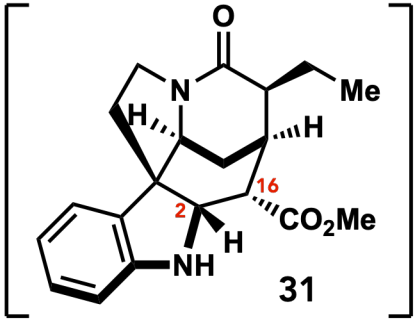


30

single diastereomer

AcOH

$NaBH_3CN$



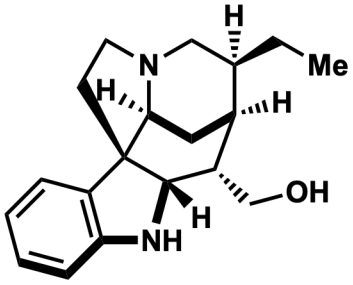
31

Red-Al

PhMe, 130 °C

75%

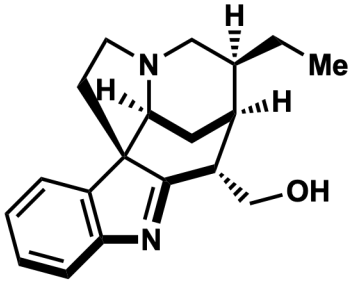
(***two steps***)



Geissoschizoline

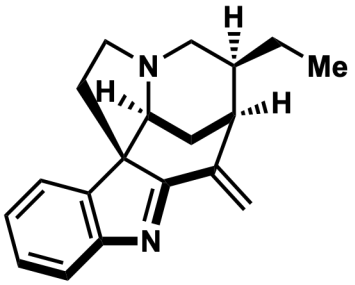
formal synthesis

(***ref. 10k***)



Dehydrogeissoschizoline

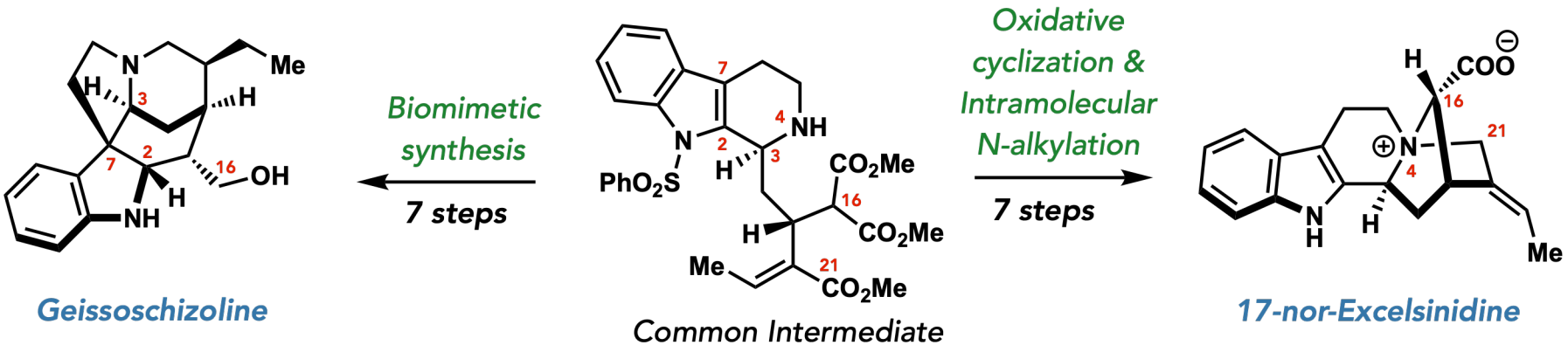
&



Dihydrovalparicine

references: *Org. Lett.* **2026**, *28*, 11720−11725; 10k) *Angew. Chem. Int. Ed.* **2015**, *54*, 12632 –12635.

Divergent Total Synthesis of 17-nor-Excelsinidine and Geissoschizoline



Summary

- Efficient and concise total synthesis of 17-*nor*-Excelsinidine and Geissoschizoline from a common intermediate
- Key steps:
  - **17-*nor*-Excelsinidine**: oxidative cyclization & intramolecular N-alkylation
  - **Geissoschizoline**: Mn-promoted oxidative cyclization/skeletal reorganization
- Including previous works, this common intermediate has successfully accessed 5 structurally distinct monoterpenoid indole alkaloid families