Ir-Catalyzed Asymmetric Total Synthesis of (-)-Communesin F

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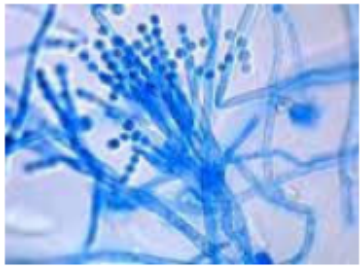
- 2008.1-现在 中国科学院昆明植物研究所，研究员
- 2010-2015 中国科学院“百人计划”

1. Xiao Liang, Shi-Zhi Jiang, Kun Wei, **Yu-Rong Yang***. “Enantioselective Total Synthesis of (−)-Alstoscholarisine A” *J. Am. Chem. Soc.* **2016**, *138*, 2560-2562.
2. Shi-Zhi Jiang, Xue-Yi Zeng, Xiao Liang, Ting Lei, Kun Wei, **Yu-Rong Yang***. “Iridium-Catalyzed Enantioselective Indole C yclization: Application to the Total Synthesis and Absolute Stereochemical Assignment of (−)-Aspidophylline A” *Angew. C hem. Int. Ed.* **2016**, *55*, 4044-4048.
3. Xiao Liang, Kun Wei*, **Yu-Rong Yang***. “Iridium-Catalyzed Enantioselective Allylation of Silyl Enol Ethers Derived from Ketones and α,β-Unsaturated Ketones” *Chem. Commun.* **2015**, 51, 17471-17474.
4. Ting Lei, Hongbin Zhang*, **Yu-Rong Yang***. “Iridium-Catalyzed Enantioselective Synthesis of (−)- and (+)-Aurantioclavin e” *Tetrahedron Lett.* **2015**, *56*, 5933-5936.

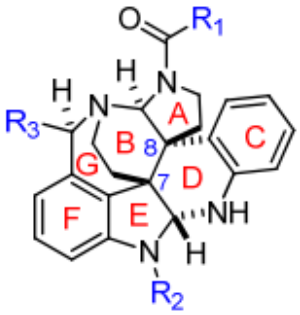
Communesin Familly

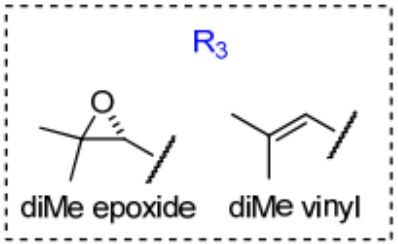


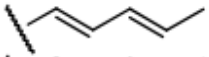
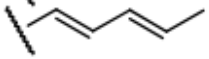
Penicillium

Marine alga *Enteromorpha Intestinalis*

- Emerging class of metabolites isolated from different marine and terrestrial species of the genus *Penicillium*.
- Communesins A and B first identified in 1993 by Numata from a strain of *Penicillium* sp. isolated from the marine algae *Enteromorpha intestinalis*.
- 8 members disclosed to date (communesins A-H).
- Indole polycyclic alkaloids with:
  - 2 vicinal quaternary centers at C7/8
  - 2 aminal moieties.
- Biological activity:
  - moderate antiproliferative activity against several human leukemia cell lines
  - active against brine shrimps
  - antihelmintic activity
  - insecticidal activity against silkworms
  - microfilaments disruption.



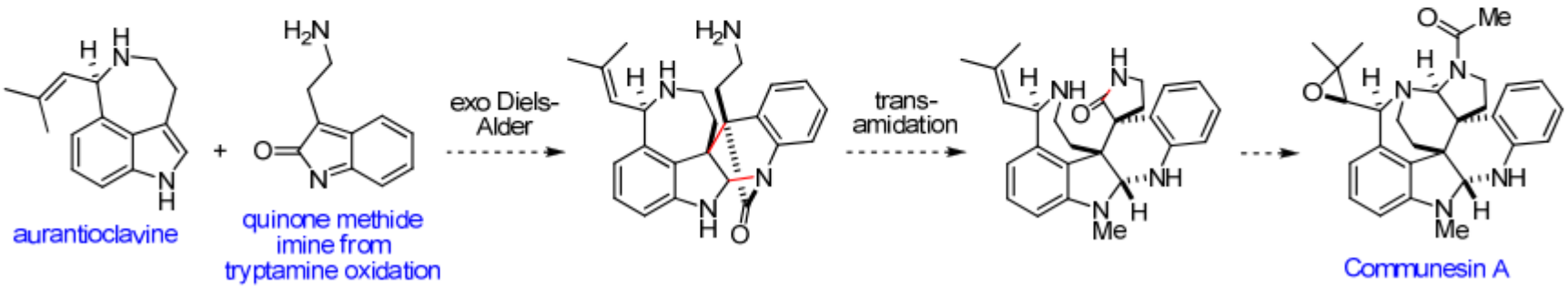


	R_1	R_2	R_3
Communesin A	Me	Me	diMe epoxide
Communesin B		Me	diMe epoxide
Communesin C		H	diMe epoxide
Communesin D		CHO	diMe epoxide
Communesin E	Me	H	diMe epoxide
Communesin F	Me	Me	diMe vinyl
Communesin G	Et	Me	diMe epoxide
Communesin H	*n*-Pr	Me	diMe epoxide

Numata, A.; Takahashi, C.; Ito, Y.; Takada, T.; Kawai, K.; Usami, Y.; Matsumura, E.; Imachi, M.; Ito, T.; Hasegawa, T. *Tetrahedron Lett.* **1993**, *34*, 2355. Jadulco, R.; Edrada, R. A.; Ebel, R.; Berg, A.; Schauman, K.; Wray, V.; Steube, K.; Proksch, P. *J. Nat. Prod.* **2004**, *67*, 78. Hayashi, H.; Matsumoto, H.; Akiyama, K. *Biosci., Biotechnol., Biochem.* **2004**, *68*, 753. Dalsgaard, P. W.; Blunt, J. W.; Munro, M. H. G.; Frisvad, J. C.; Christophersen, C. *J. Nat. Prod.* **2005**, *68*, 258. Kerzaon, I.; Pouchus, Y. F.; Monteau, F.; Le Bizec, B.; Nourrisson, M. R.; Biard, J. F.; Grovel, O. *Rapid Commun. Mass Spectrom.* **2009**, *23*, 3928.

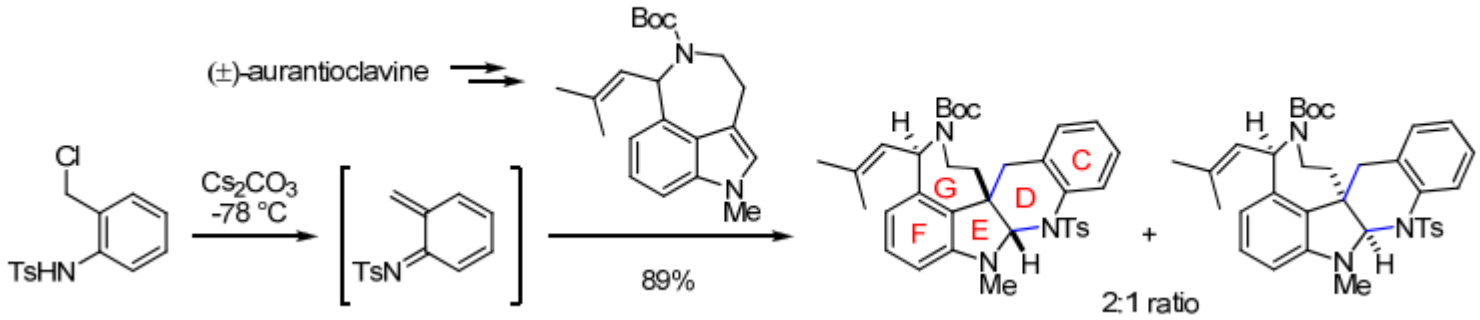
Communesins: Proposed Biosynthetic Pathways

- Stoltz and co-workers (2003)



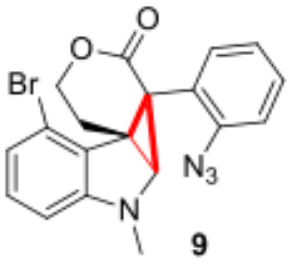
May, J. A.; Zeidan, R. K.; Stoltz, B. M. *Tetrahedron Lett.* **2003**, *44*, 1203.

- Stoltz and May (2006): Biomimetic model study of inverse-demand Diels-Alder



May, J. A.; Stoltz, B. M. *Tetrahedron* **2006**, *62*, 5262.

Highlights of the strategies in the synthesis of communesin F



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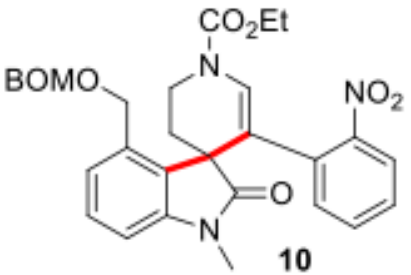
(Qin, 2007)



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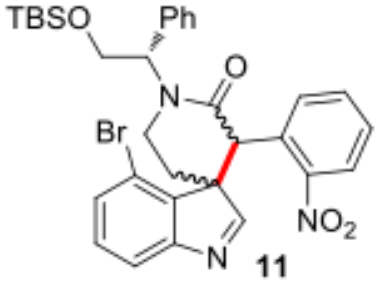
(Weinreb, 2009)



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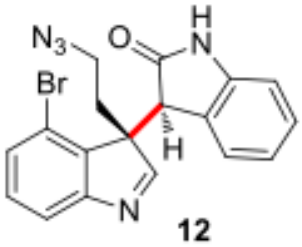
(Ma, 2010)



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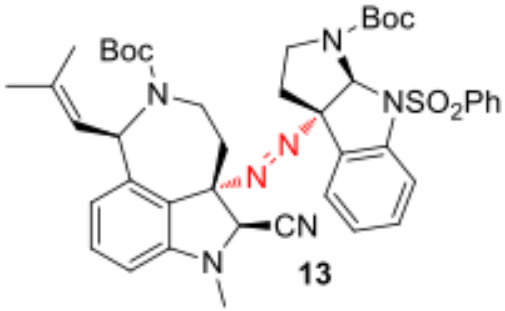
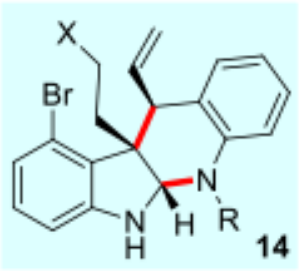
(Funk, 2012)



13

(Movassaghi, 2016)

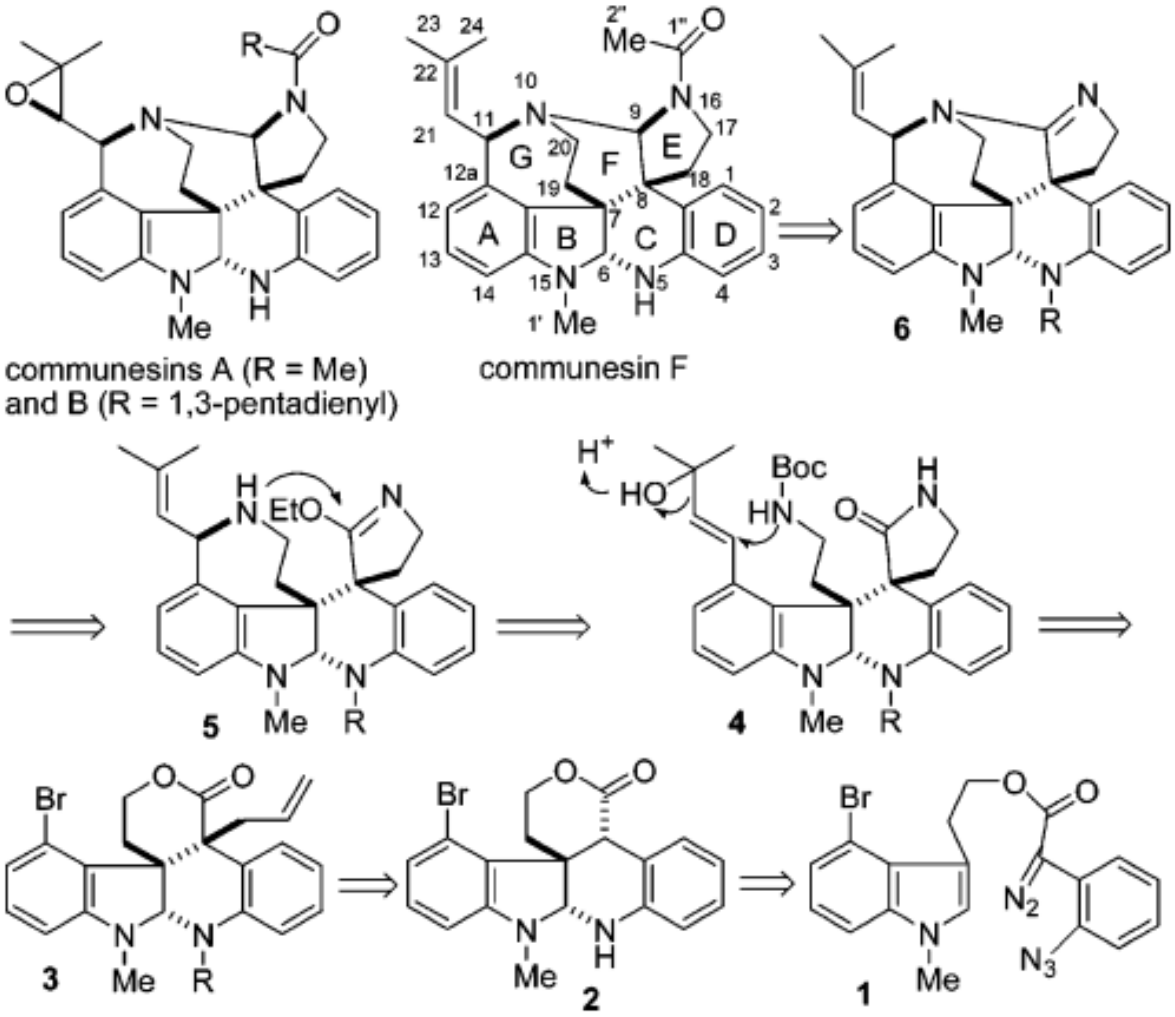


14

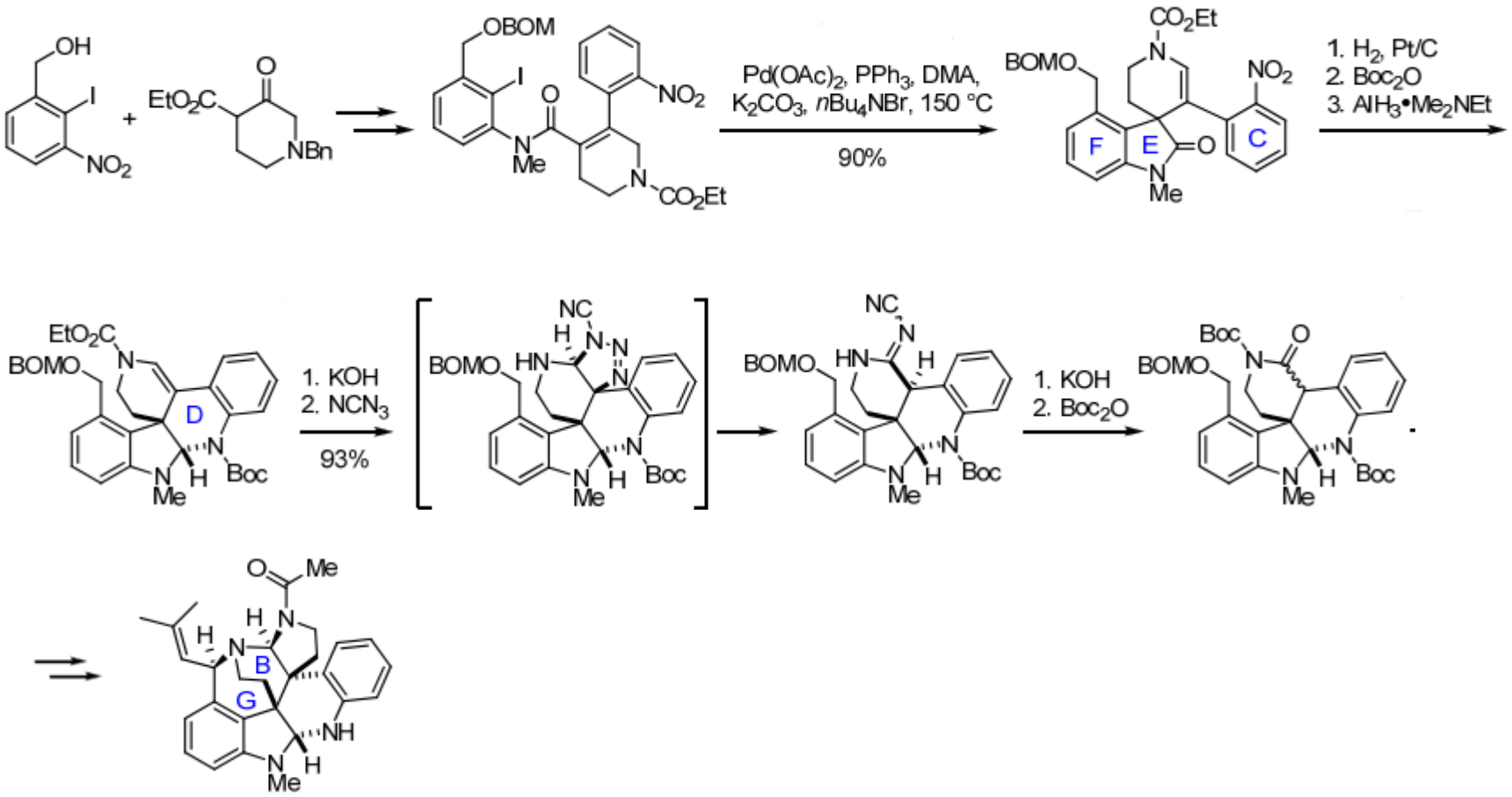
this work

one step?
catalytic,
asymmetric?

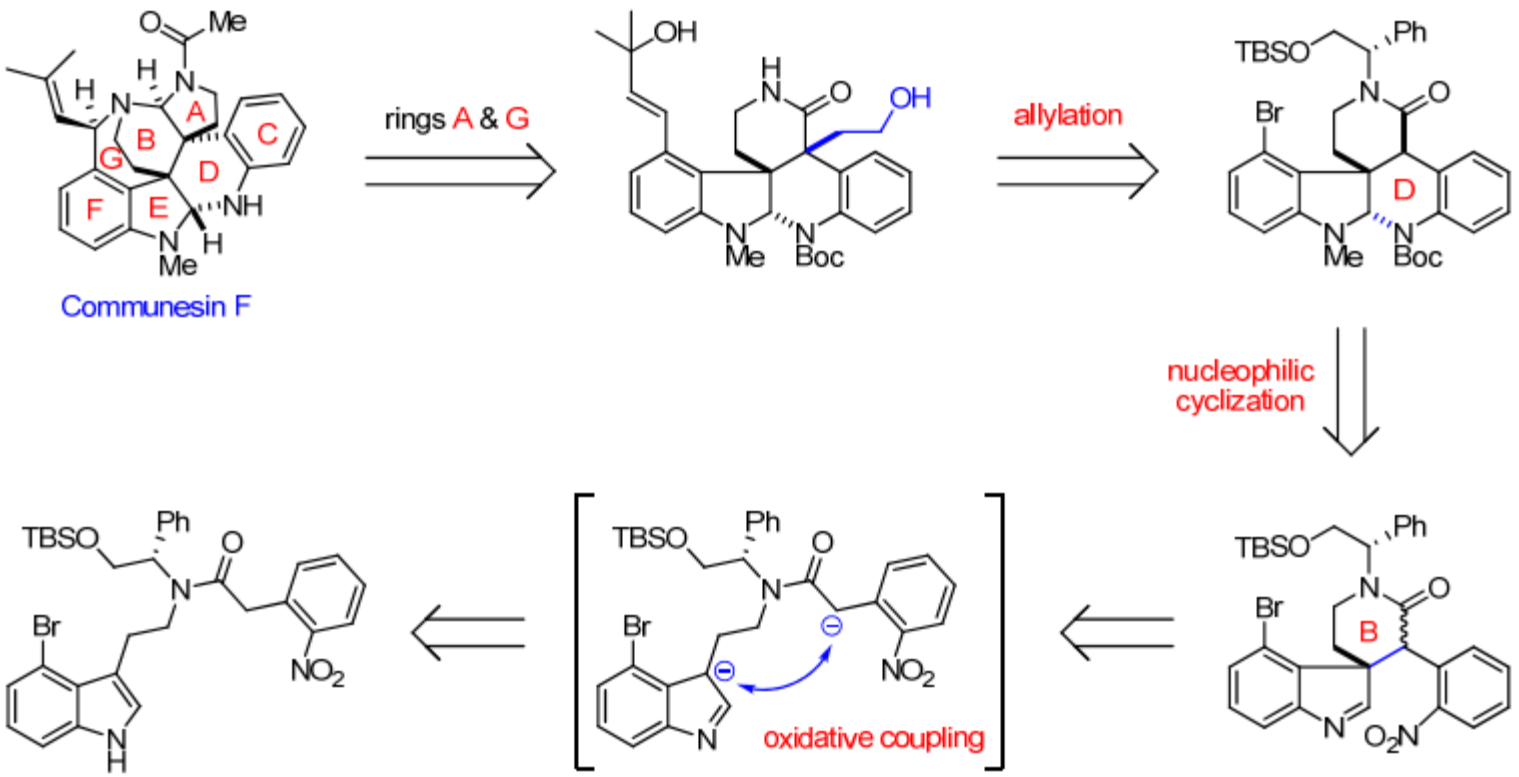
(±)-Communesin F：Qin’s synthesis (2007)



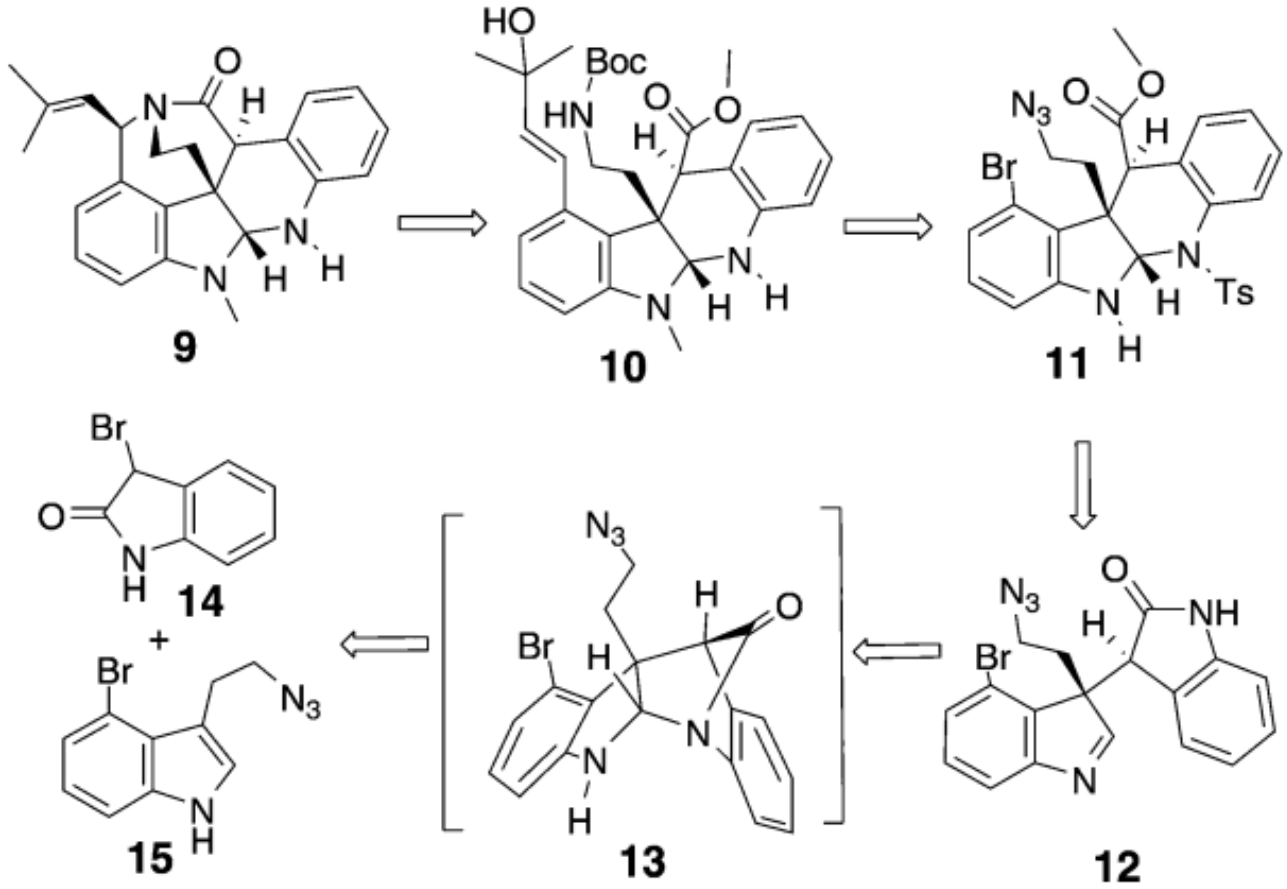
(±)- Communesin F：Weinreb's synthesis (2009)



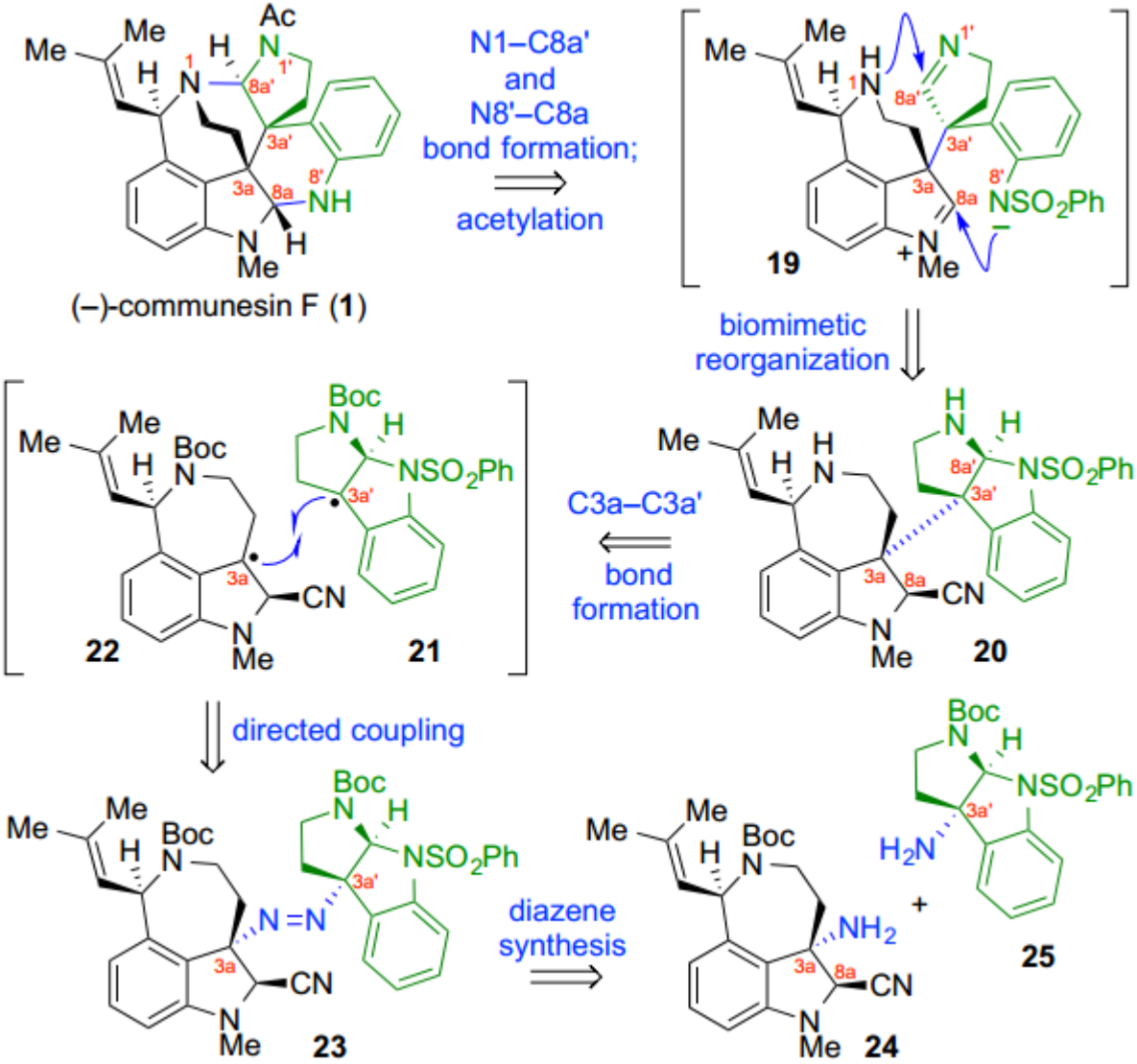
(-)-Communesin F：Ma’s synthesis (2010)



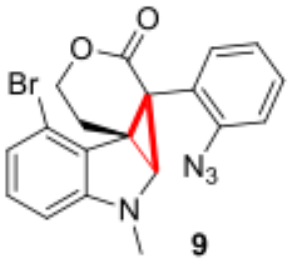
(±)-Communesin F：Funk’s synthesis (2012)



(-)-Communesin F：Movassaghi's synthesis (2016)



Highlights of the strategies in the synthesis of communesin F



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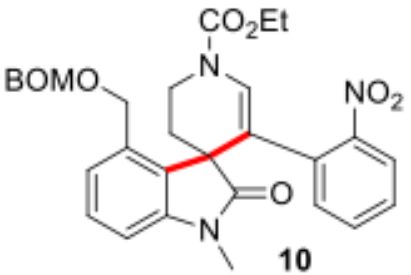
(Qin, 2007)



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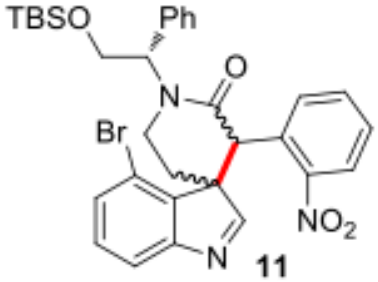
(Weinreb, 2009)



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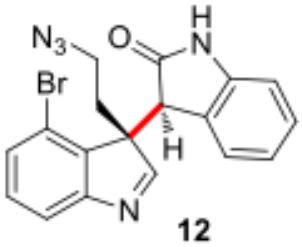

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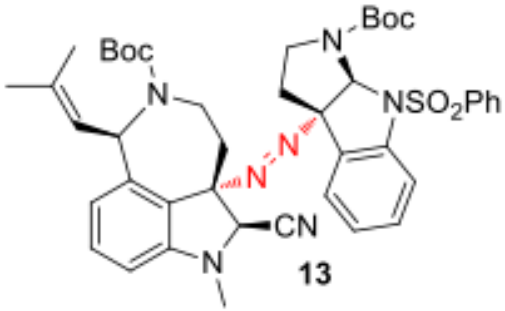

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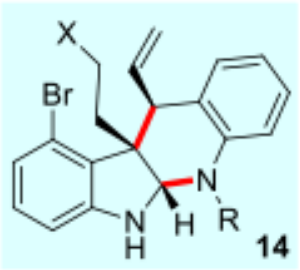

14

this work

one step?
catalytic,
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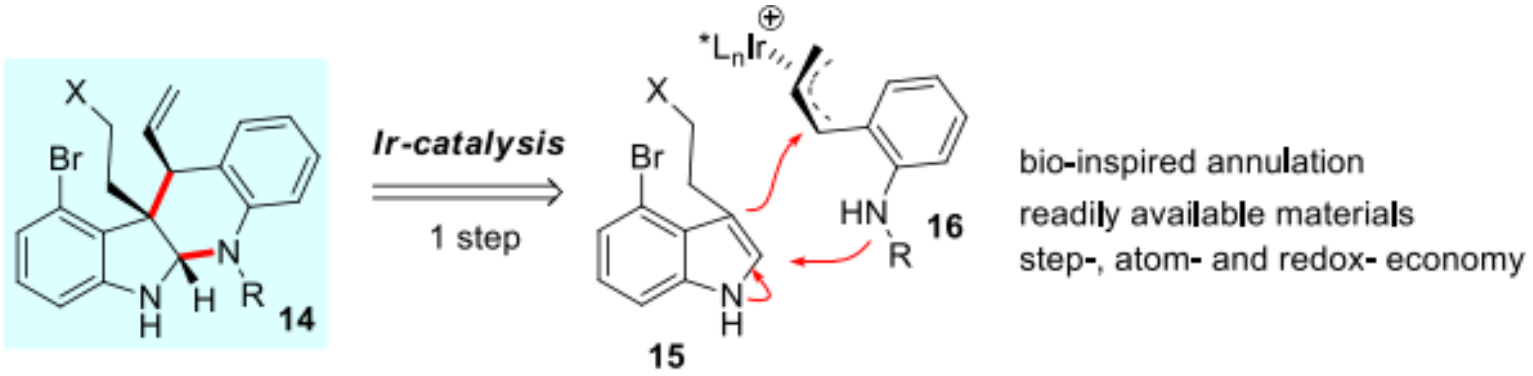
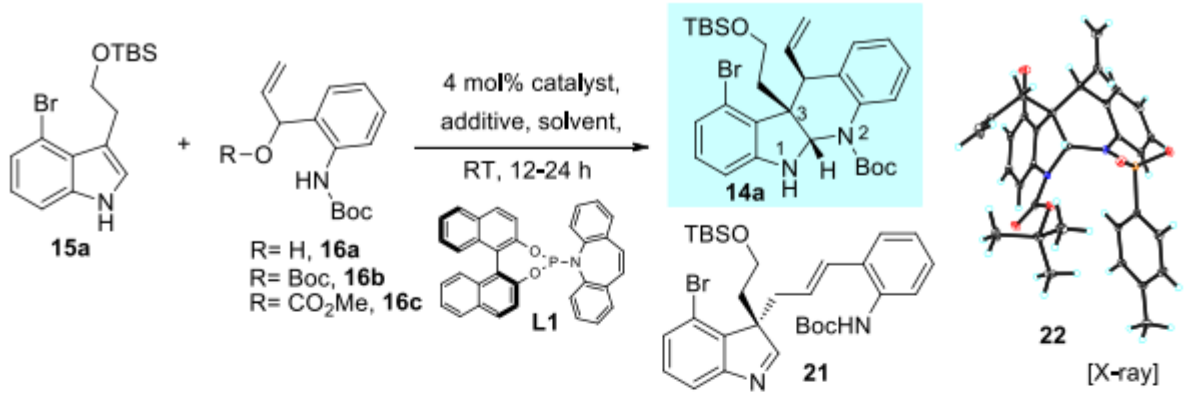
Design of Ir-Catalyzed Asymmetric Cyclization Approach to Tetracyclic Aminal.

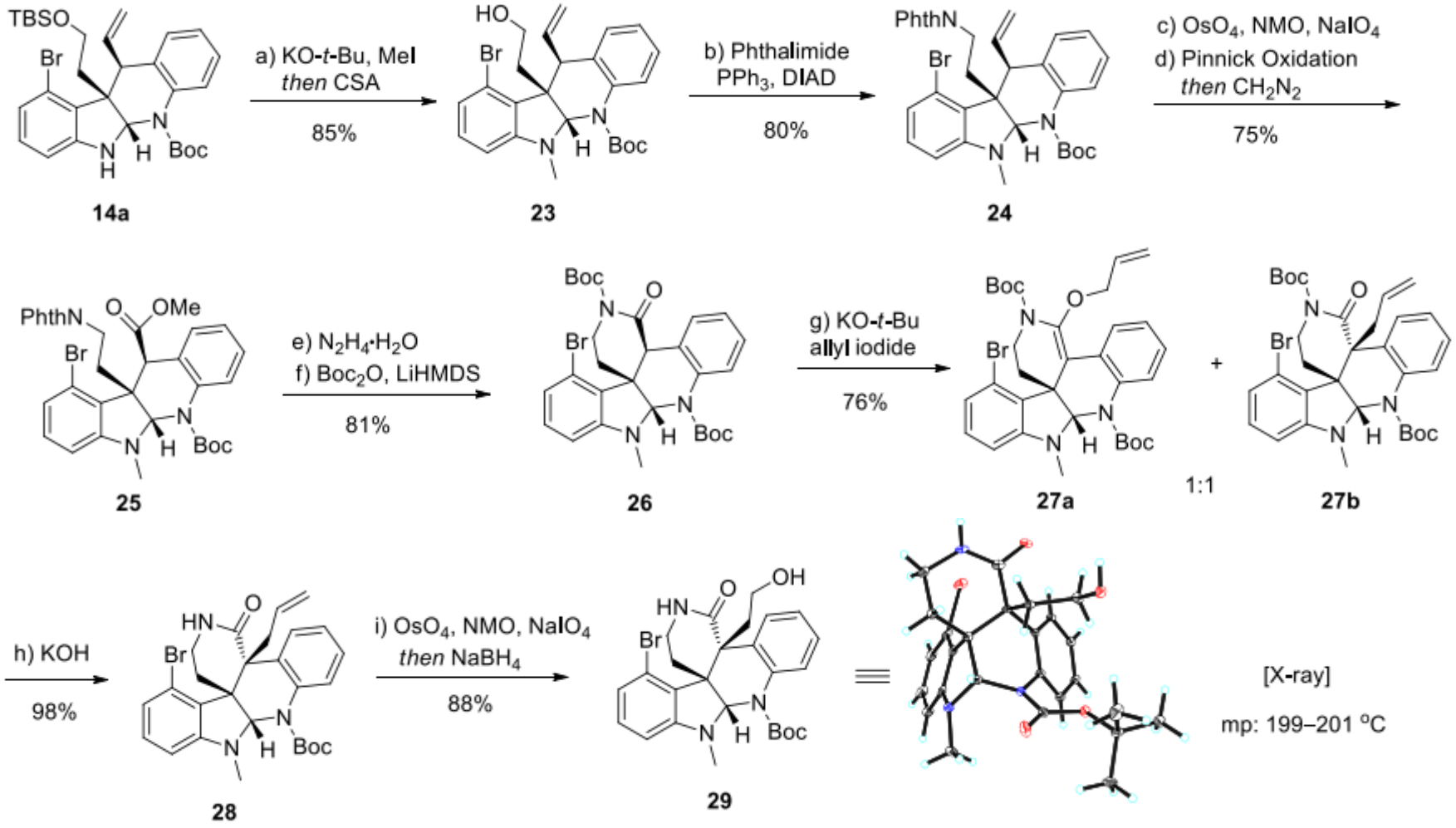


Optimization of the Catalyst and Additives Used for the Annulation of *N, N*-aminal-Containing Tetracycle

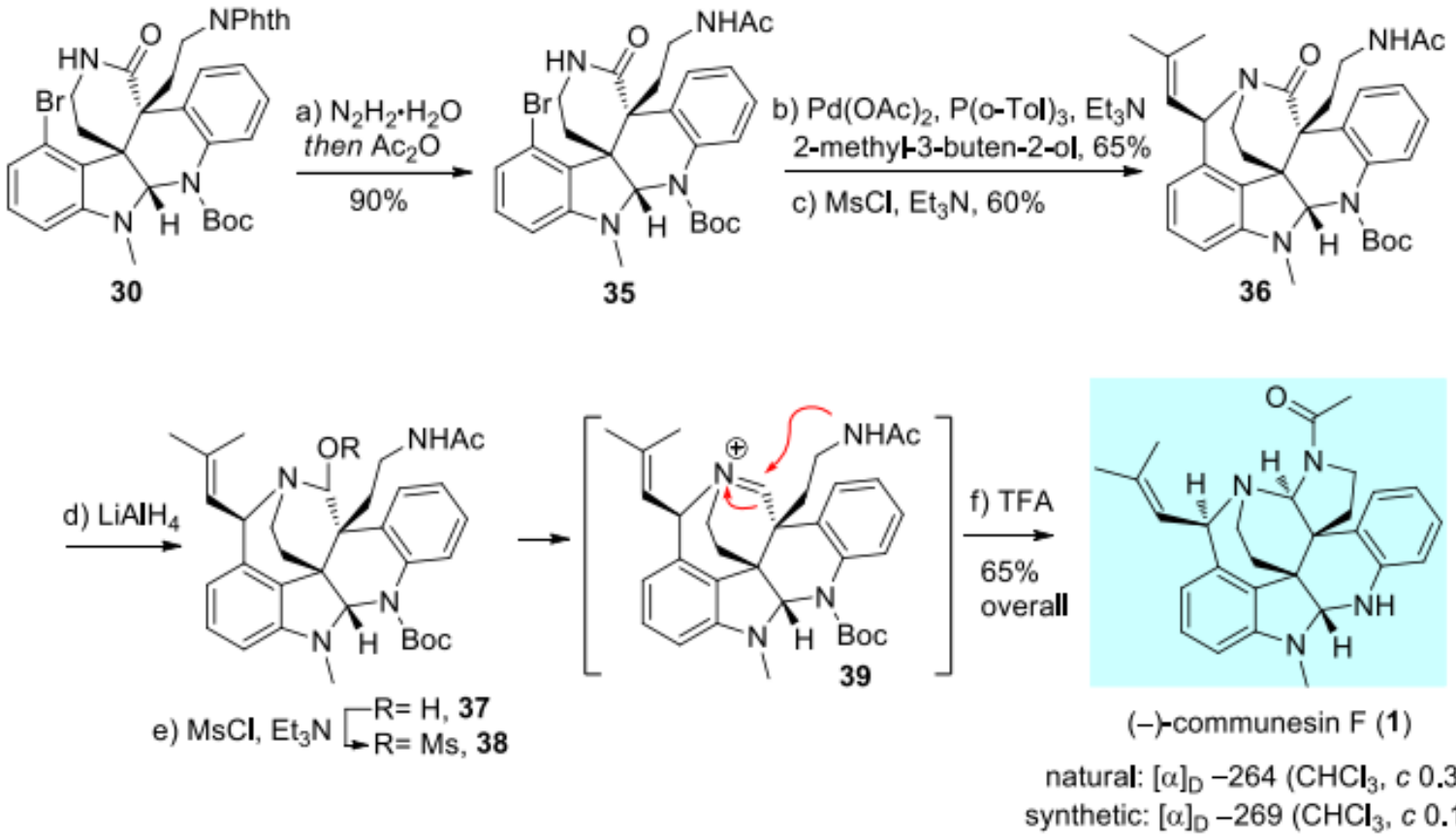


6	$[Ir(cod)Cl]_2$ (S)-**L1**	Et_3B, KO-*t*-Bu	THF	6:1	91	52
7	$[Ir(cod)Cl]_2$ (S)-**L1**	Et_3B, KO-*t*-Bu	toluene	>10:1	92	65
8[g]	$[Ir(cod)Cl]_2$ (S)-**L1**	Et_3B, KO-*t*-Bu	toluene	>10:1	83	65
9	$[Ir(cod)Cl]_2$ (S)-**L1**	Ph_3B, KO-*t*-Bu	toluene	-	-	trace
10	$[Ir(cod)Cl]_2$ (S)-**L1**	9-BBN-*n*-C_6H_{13}, KO-*t*-Bu	toluene	>10:1	99	55
11[h]	$[Ir(cod)Cl]_2$ (S)-**L1**	9-BBN-*n*-C_6H_{13}, KO-*t*-Bu	toluene	>10:1	93	56

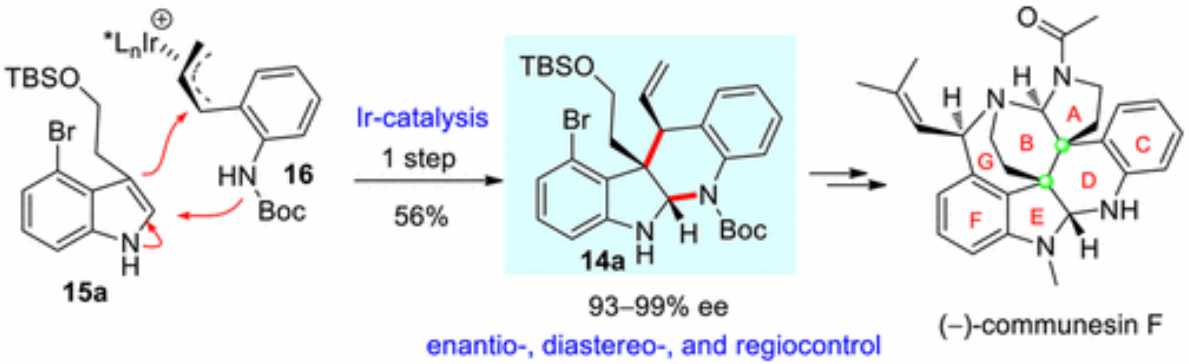
Synthesis of the Pentacyclic Intermediates



Completion of the Total Synthesis of (-)-Communesin F



Conclusion



- An enantio-, diastereo-, and regioselective iridium-catalyzed annulation between a 3-substituted indole and a protected 2-aminophenyl allylic electrophile, constructing the lower *N,N*-aminal-containing CDEF tetracyclic core within one step.