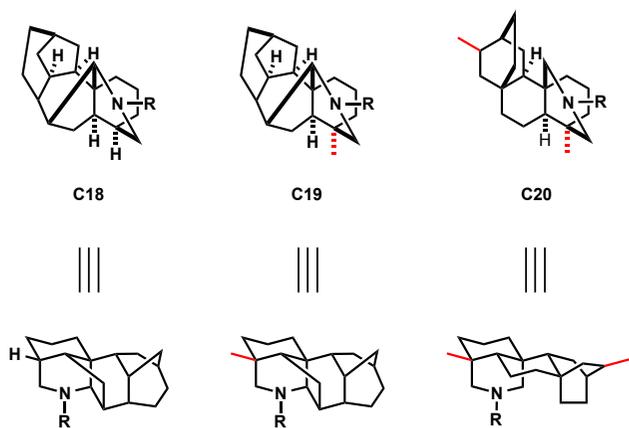


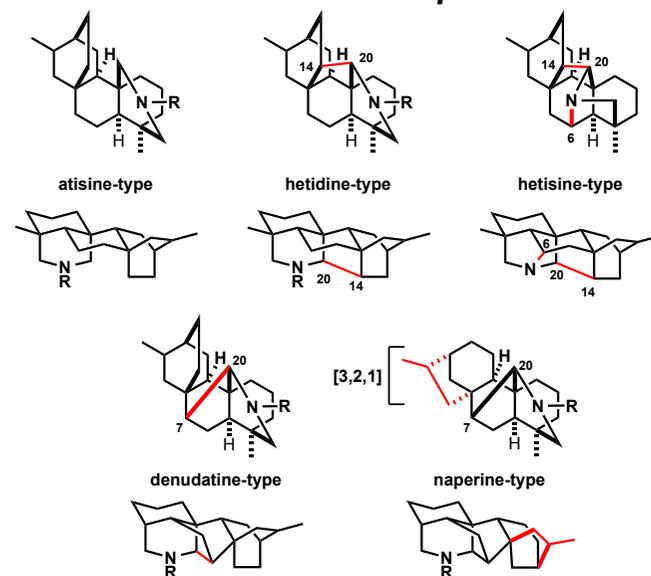
Brief Introduction of Diterpenoid Alkaloids



Wang, F.-P.; Chen, Q.-H.; Liu, X. -Y. *Mat. Prod. Rep.* 2010, 27, 529.

1

Classification of C20-Diterpene Alkaloids



Wang, F.-P.; Chen, Q.-H.; Liu, X. -Y. *Nat. Prod. Rep.* 2010, 27, 529.

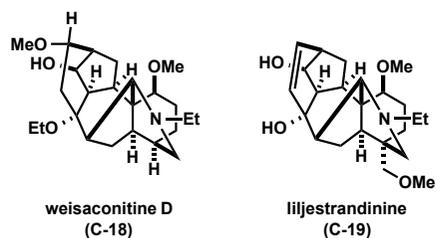
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Contents

1. Recent Synthetic Study of C20-Diterpene Alkaloids



2. Total Synthesis of weisaconitine D and liljestrandinine



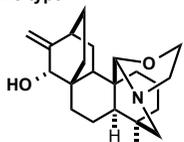
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1. Recent Synthetic Study of C20-Diterpene Alkaloids

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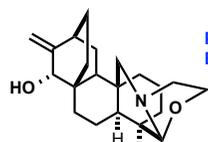
Previous Synthesis of C20 Diterpene Alkaloids

atisine-type



atisine

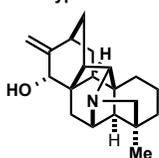
Pelletier (1956)
Nagata (1963)
Masanune (1964)
Tahara (1966)
Fukumoto (1988)
Wiesner (1966)
Wang (2012)



isoatisine

Pelletier (1956)
Baran (2014)

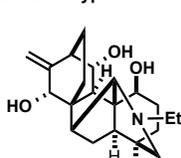
hetisine-type



nominine

Muratake (2004)
Gin (2006)

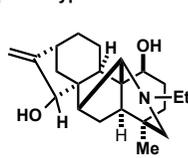
denudatine-type



lepenine

Fukuyama (2014)

naperine-type



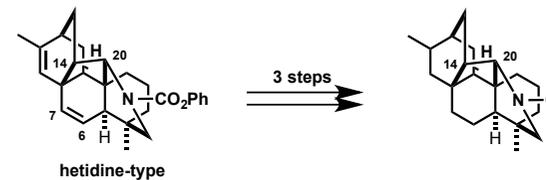
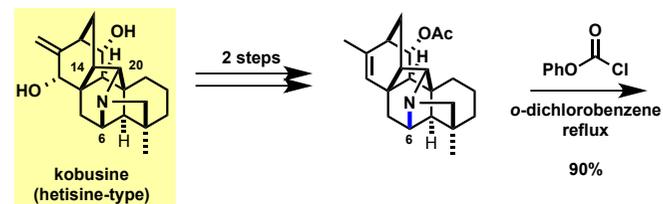
napelline

Wiesner (1980)

Review on total synthesis of C20 diterpene alkaloids:
Liu, X. -Y.; Qin, T. *Asian J. Org. Chem.* 2015, 4, 2010.

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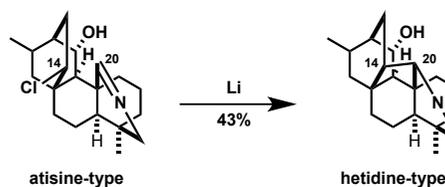
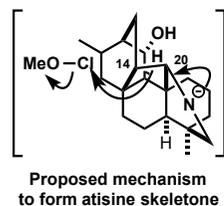
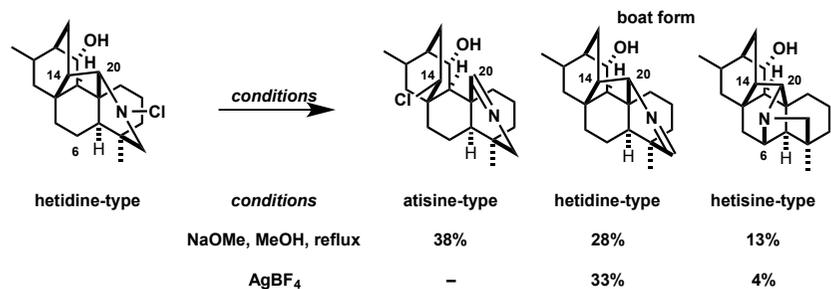
C6-N Bond Fragmentation



Yatsunami, T.; Isono, T.; Hayakawa, I.; Okamoto, T. *Chem. Pharm. Bull.* 1975, 3030
Okamoto, T. *Chem. Pharm. Bull.* 1978, 3199.

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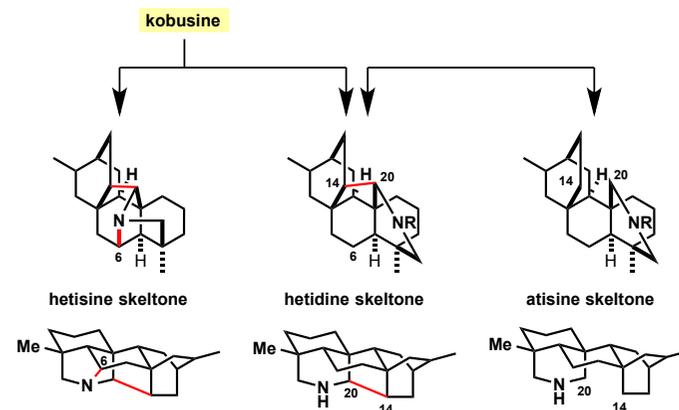
Transformation of Chloramine



Yatsunami, T.; Isono, T.; Hayakawa, I.; Okamoto, T. *Chem. Pharm. Bull.* 1975, 3030
Okamoto, T. *Chem. Pharm. Bull.* 1978, 3199.

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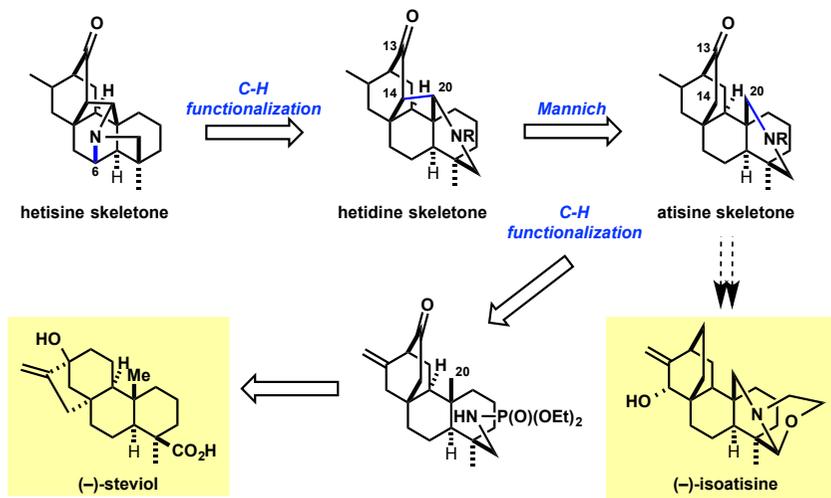
Unified Strategies for C20-Diterpene Alkaloids



Cherney, E. C.; Lopchuk, L. M.; Green, J. C.; Baran, P. S. *J. Am. Chem. Soc.* 2014, 136, 12592.

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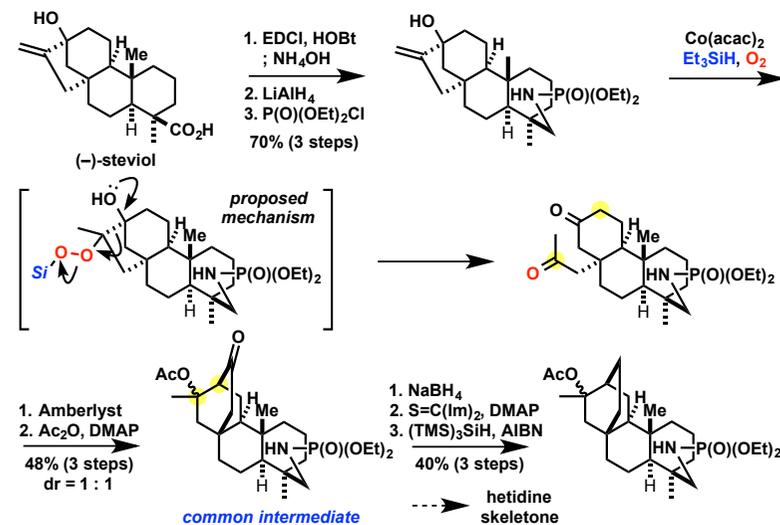
Baran's Retrosynthetic Analysis



Cherney, E. C.; Lopchuk, L. M.; Green, J. C.; Baran, P. S. *J. Am. Chem. Soc.* 2014, 136, 12592.

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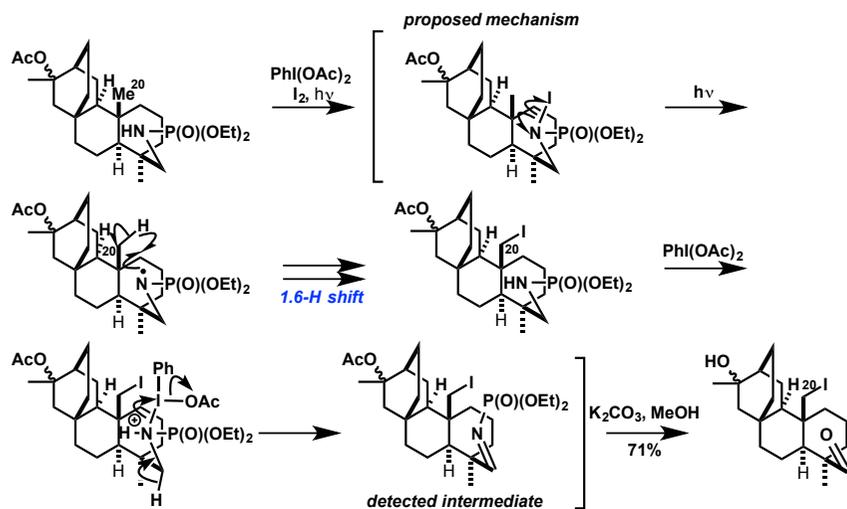
Construction of Bicyclo[2,2,2]-Skeleton



Cherney, E. C.; Lopchuk, L. M.; Green, J. C.; Baran, P. S. *J. Am. Chem. Soc.* 2014, 136, 12592.

10

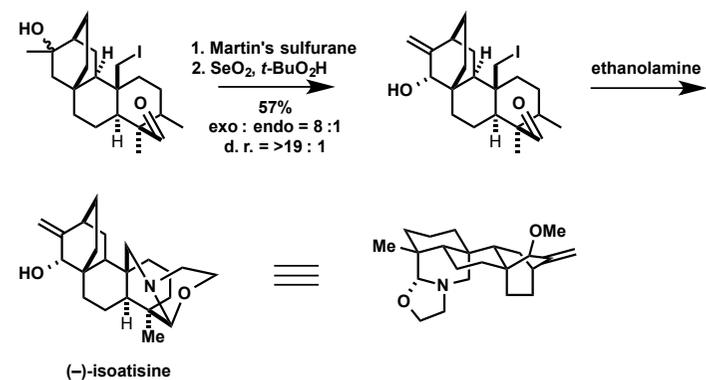
Hofmann-Löffler-Freytag reaction



Cherney, E. C.; Lopchuk, L. M.; Green, J. C.; Baran, P. S. *J. Am. Chem. Soc.* 2014, 136, 12592.

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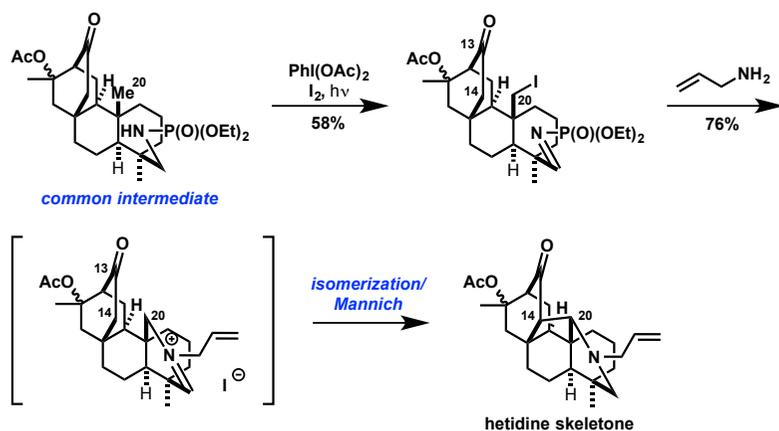
Total Synthesis of (-)-isoatisine



Cherney, E. C.; Lopchuk, L. M.; Green, J. C.; Baran, P. S. *J. Am. Chem. Soc.* 2014, 136, 12592.

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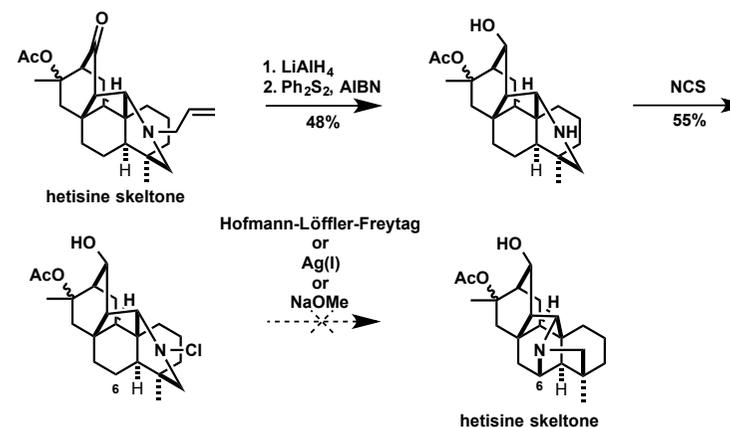
C14-C20 Bond Formation



Cherney, E. C.; Lopchuk, L. M.; Green, J. C.; Baran, P. S. *J. Am. Chem. Soc.* 2014, 136, 12592.

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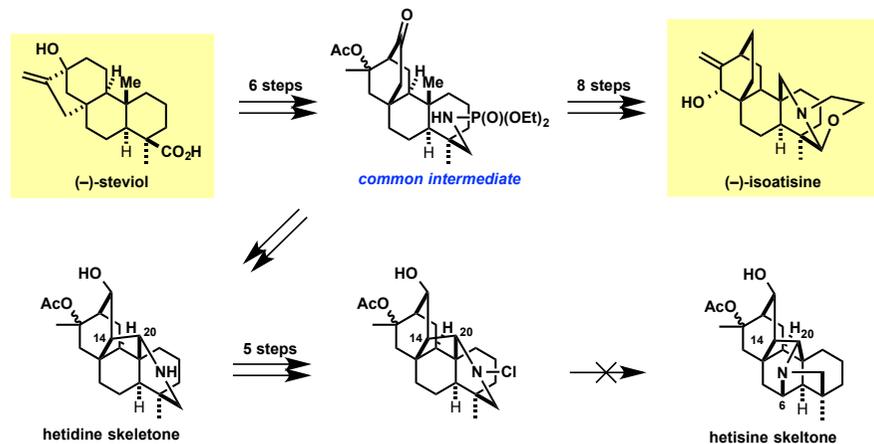
Attempt to Form N-C6 Bond



Cherney, E. C.; Lopchuk, L. M.; Green, J. C.; Baran, P. S. *J. Am. Chem. Soc.* 2014, 136, 12592.

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Short Summary

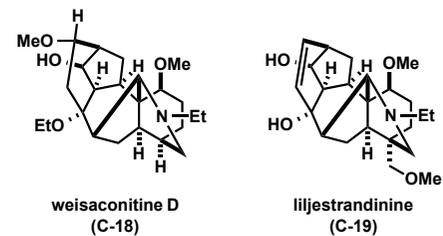


Previous reports on total synthesis of atisine-type natural products: 22-66 steps

Cherney, E. C.; Lopchuk, L. M.; Green, J. C.; Baran, P. S. *J. Am. Chem. Soc.* 2014, 136, 12592.

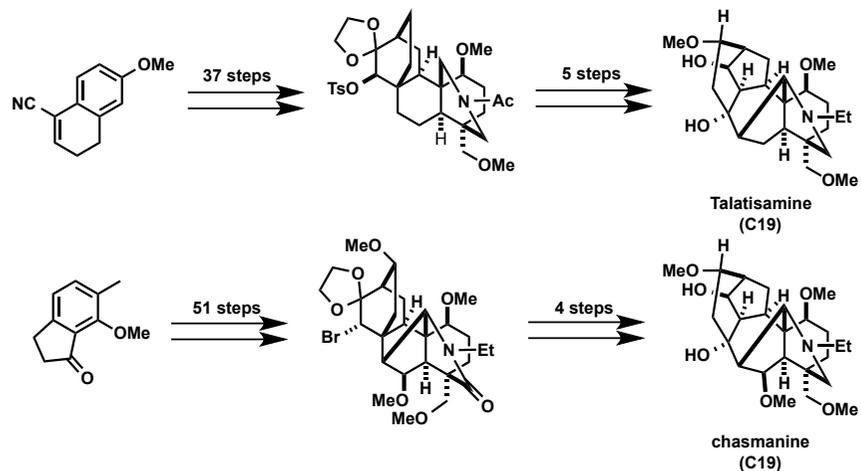
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2. Total Synthesis of weisaconitine D and liljestrandinine



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Previous Synthesis of C19 Diterpenoid Alkaloids



Total synthesis of talatisamine:

(a) Wiesner, K.; Tsai, T. Y. R.; Huber, K.; Bolton, S. E. *J. Am. Chem. Soc.* 1974, 96, 4990.

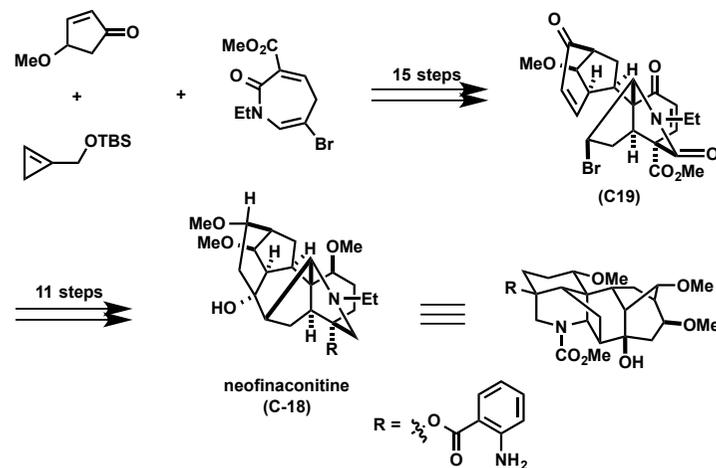
(b) Wiesner, K. *Pure Appl. Chem.* 1975, 41, 93.

Total synthesis of chasmanine:

Wiesner, K. *Pure Appl. Chem.* 1979, 51, 689.

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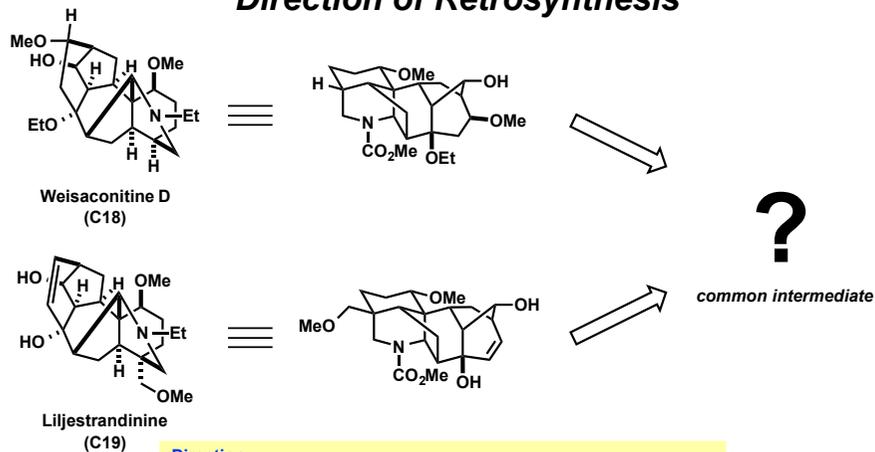
Previous Synthesis of C18 Diterpenoid Alkaloids



Shi, Y. Wilmot, J. T.; Nordstrøm, L. U.; Tan, D. S.; Gin, D. Y. *J. Am. Chem. Soc.* 2013, 135, 14313.

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Direction of Retrosynthesis

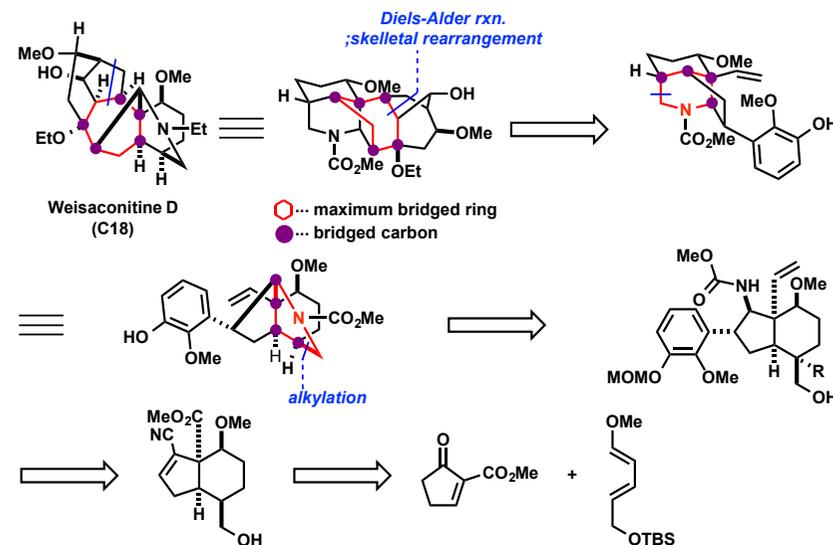


Direction:

To achieve maximal simplification of the bridged cyclic system, the maximum bridged ring should be constructed at later stage.

Corey et. al. *JACS*, 1975, 1817.

Retrosynthetic Analysis



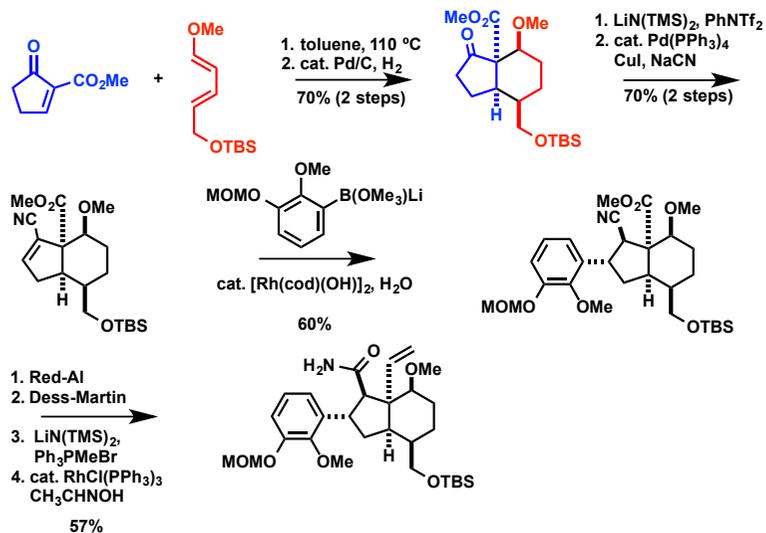
Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493.

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Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493.

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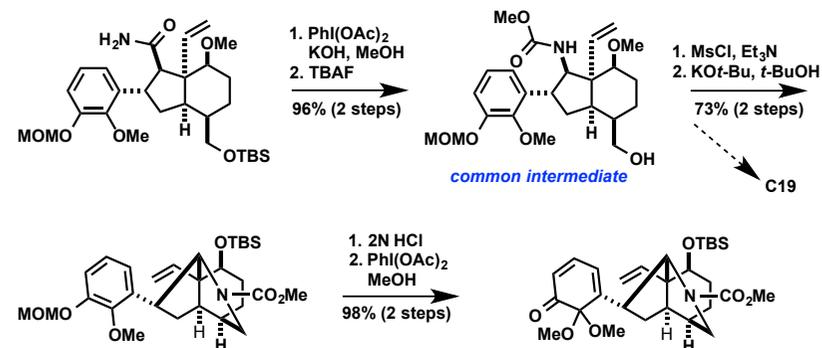
Synthesis of 6/5- Ring



Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493.

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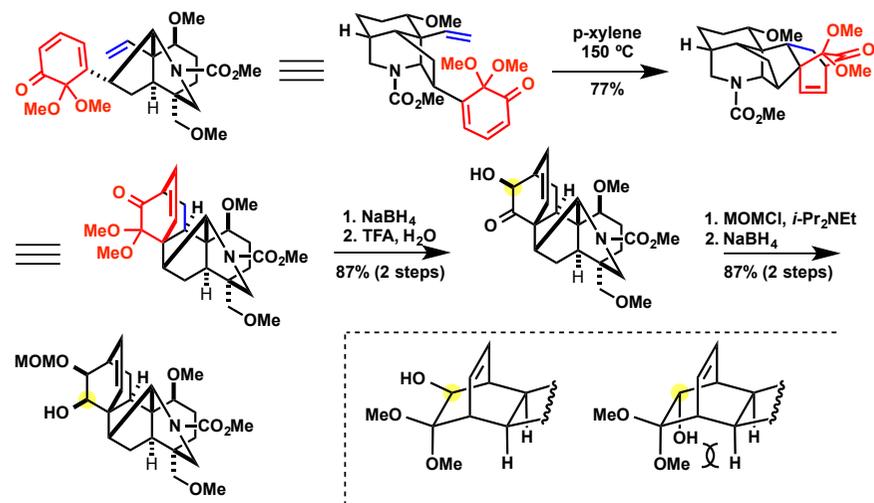
Synthesis of D.A. Precursor



Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493.

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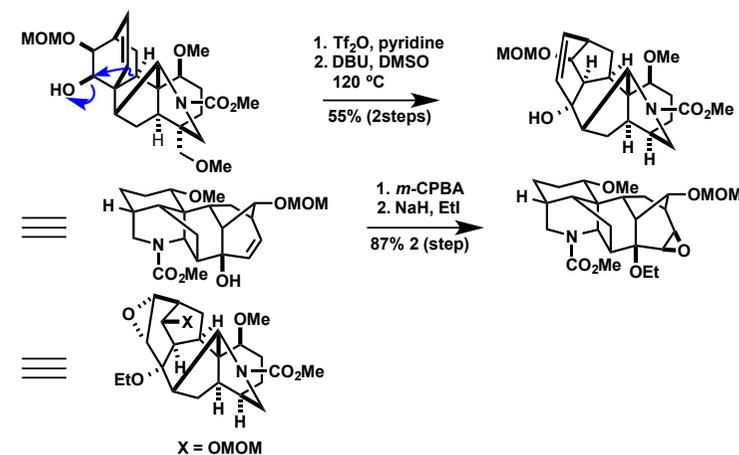
Construction of Bicyclo[2,2,2]octane Skeleton



Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493.

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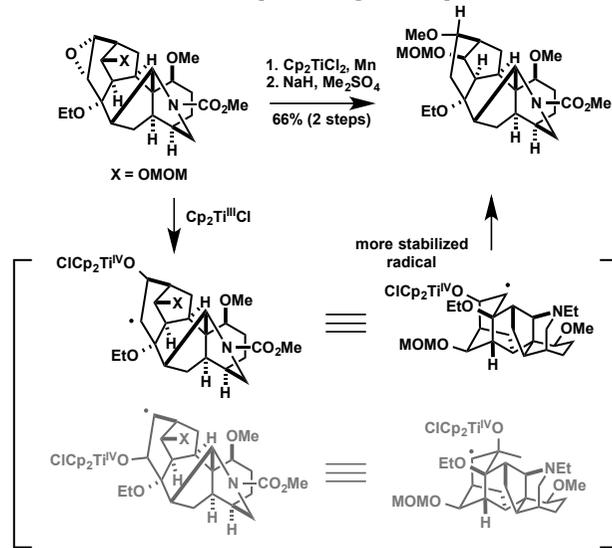
Skeletal Rearrangement



Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493.

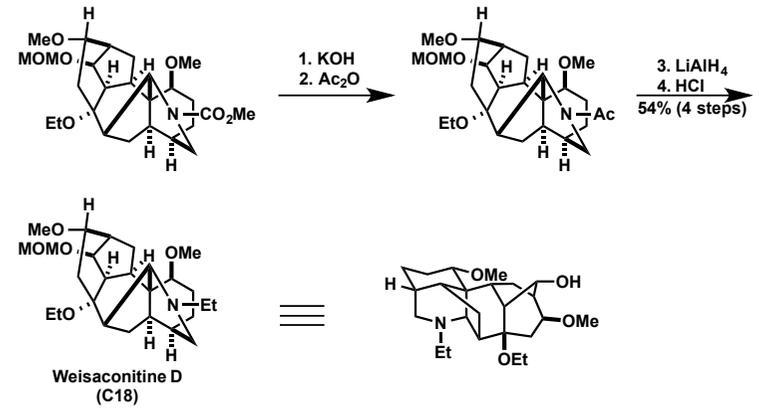
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Reductive Opening of Epoxide



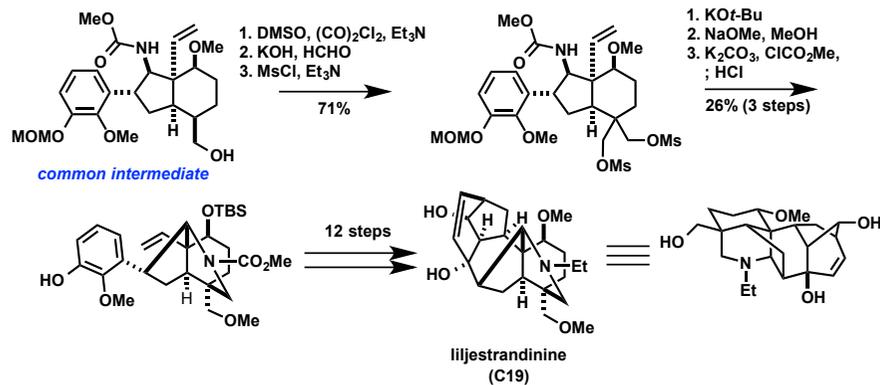
Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493. 25

Total Synthesis of Weisaconitine D



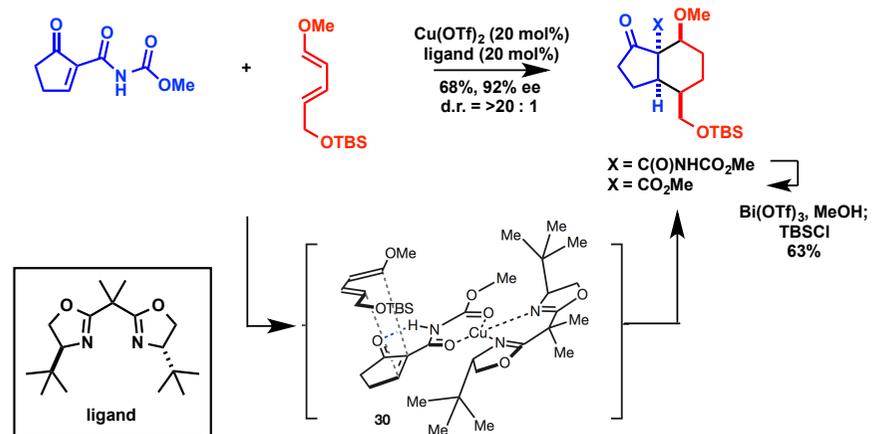
Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493. 26

Total Synthesis of Iijestrandinine



Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493. 27

Enantioselective Diels-Alder Reaction



Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M. Qin, J.; Lilien, R.; Sarpong, R. *Nature*, 2015, 528, 493. 28

