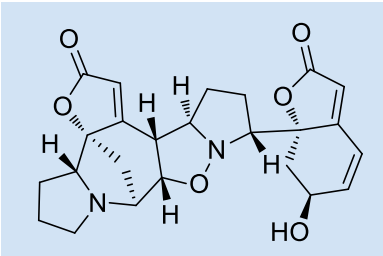
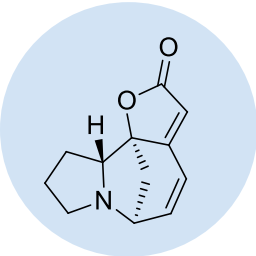
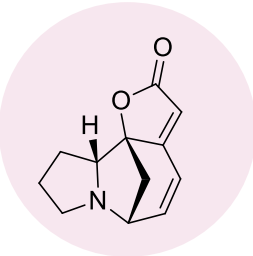
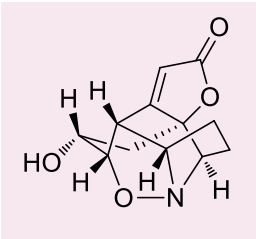
Total Synthesis of (-)-Flueggine A And (+)-Virosaine B

Wei, H., Qiao, C., Liu, G., Yang, Z. and Li, C.-c. *Angew. Chem. Int. Ed.*, **2013**, *52*: 620–624.

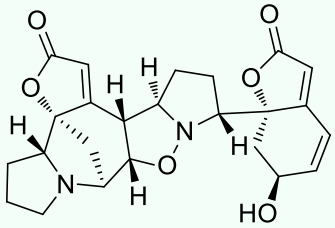
Yongzhao Yan

Current lit.

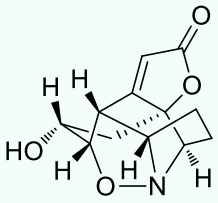
2013.2.23

(-)-Flueggine A And (+)-Virosaine B

- Isolated from the twigs and leaves of *Flueggea virosa.*
- The structures and absolute configurations of ***(-)-Flueggine A*** and ***(+)-Virosaine B*** were elucidated by means of NMR, X-ray diffraction and CD analyses.[2,3]



(-)-Flueggine A



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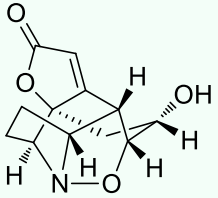
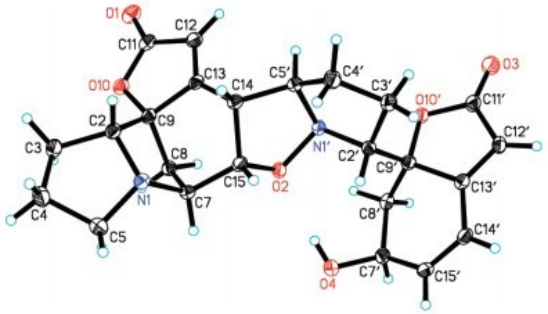
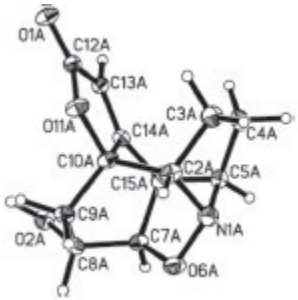


(-)-Virosaine A

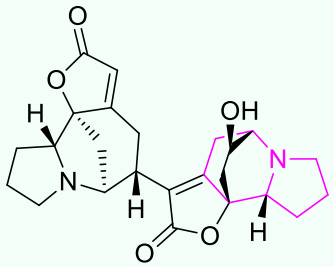




1. Picture source: http://blog.roodo.com/ato543/archives/9925831.html
2. B. X. Zhao, Y. Wang, D. M. Zhang, R. W. Jiang, G. C. Wang, J. M. Shi, X. J. Huang, W. M. Chen, C. T. Che, W. C. Ye, *Org. Lett.* 2011,**13**, 3888.
3. B. X. Zhao, Y. Wang, D. M. Zhang, X. J. Huang, L. L. Bai, Y. Yan, J. M. Chen, T. B. Lu, Y. T. Wang, Q. W. Zhang, W. C. Ye, *Org. Lett.*2012, **14**, 3096.

Biological Activities

- ***Flueggine A*** exhibited modest activities in three breast cancer cell lines, with IC_{50} values of 60±4 (MCF-7), 86±9 (MDA-MB-231), and 68±7 μM (MCF-7/ADR).[1]
- ***Flueggine B*** exhibited a significant inhibitory activity on the growth of MCF-7 and MDA-MB-231 cells, with IC_{50} values of 135±5 and 147±3 nM.
- Neither ***Virosaine A*** nor ***B*** showed cytotoxic activity against MCF-7, MDA-MB-231, HepG2, HepG2/ADM, HL-60, K562, and Hep2 cells.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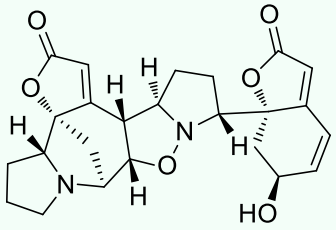
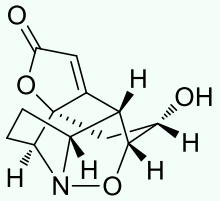
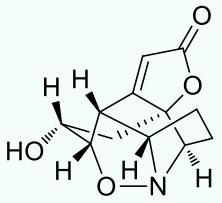

(-)-Flueggine A


(-)-Virosaine A


(+)-Virosaine B

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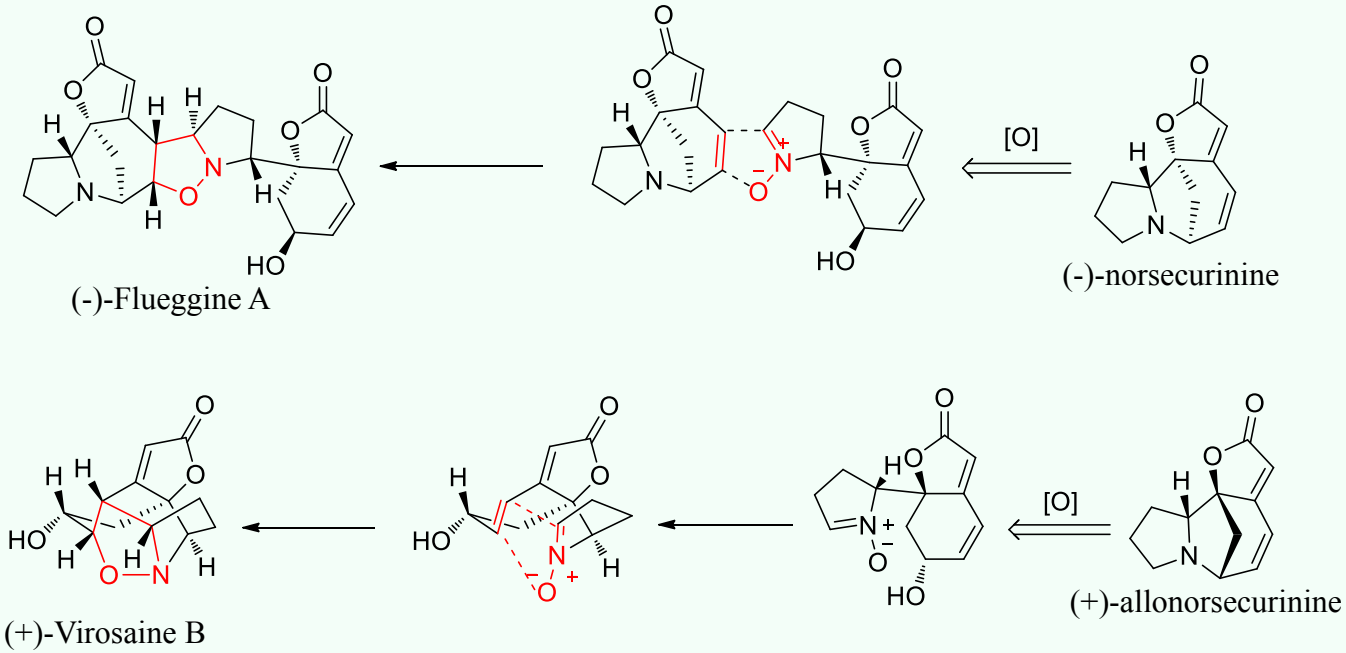
2. B. X. Zhao, Y. Wang, D. M. Zhang, X. J. Huang, L. L. Bai, Y. Yan, J. M. Chen, T. B. Lu, Y. T. Wang, Q. W. Zhang, W. C. Ye, *Org. Lett.*2012, **14**, 3096.

Proposed Biosynthetic Pathways



(-)-Flueggine A

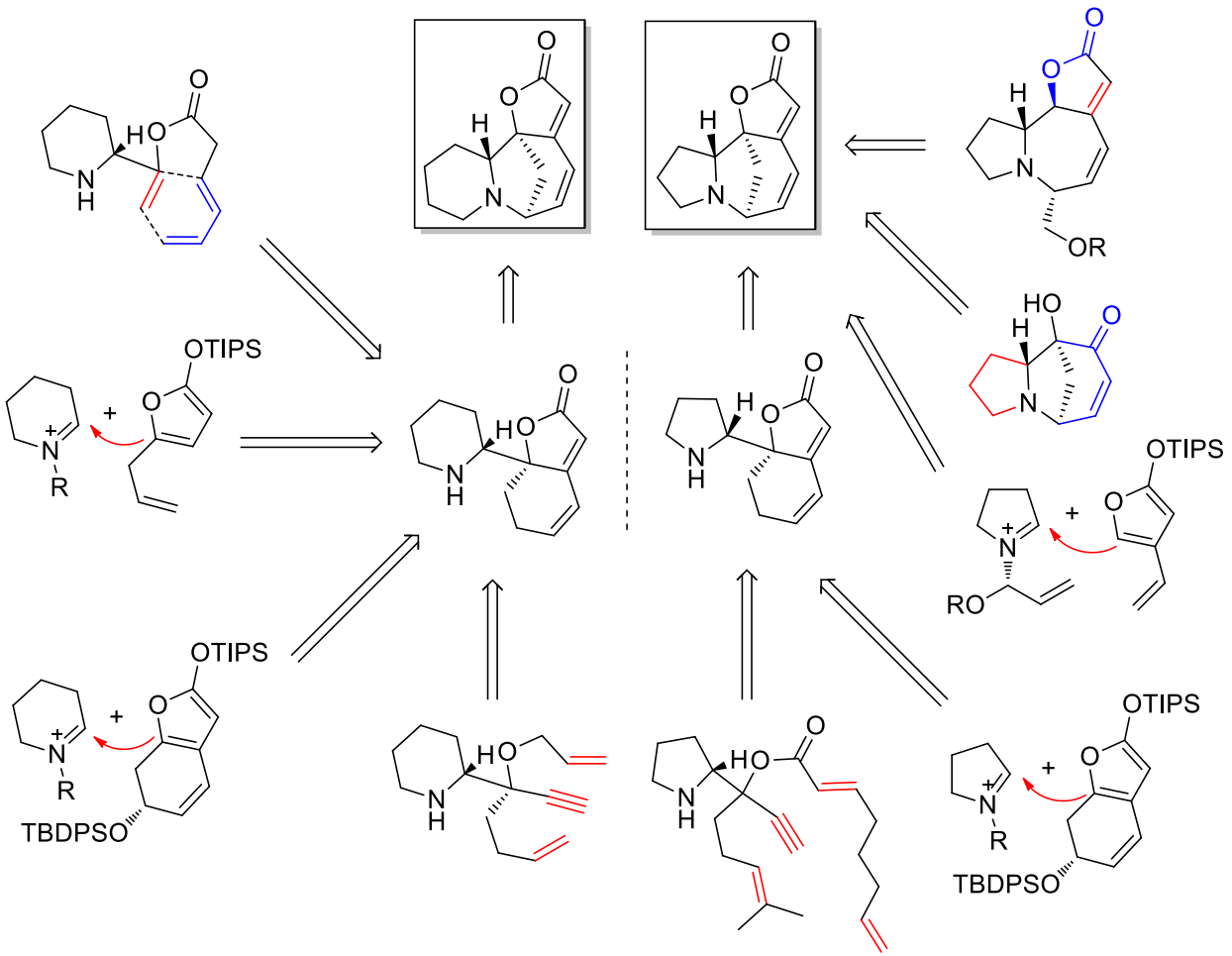
(-)-norsecurinine

(+)-Virosaine B

(+)-allonorsecurinine

1. B. X. Zhao, Y. Wang, D. M. Zhang, R. W. Jiang, G. C. Wang, J. M. Shi, X. J. Huang, W. M. Chen, C. T. Che, W. C. Ye, *Org. Lett.* 2011,**13**, 3888.
2. B. X. Zhao, Y. Wang, D. M. Zhang, X. J. Huang, L. L. Bai, Y. Yan, J. M. Chen, T. B. Lu, Y. T. Wang, Q. W. Zhang, W. C. Ye, *Org. Lett.*2012, **14**, 3096.

Synthesis of Securinega Alkaloids



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2. Wei, H., Qiao, C., Liu, G., Yang, Z. and Li, C.-c. *Angew. Chem. Int. Ed.*, 2013, ***52***: 620–624.
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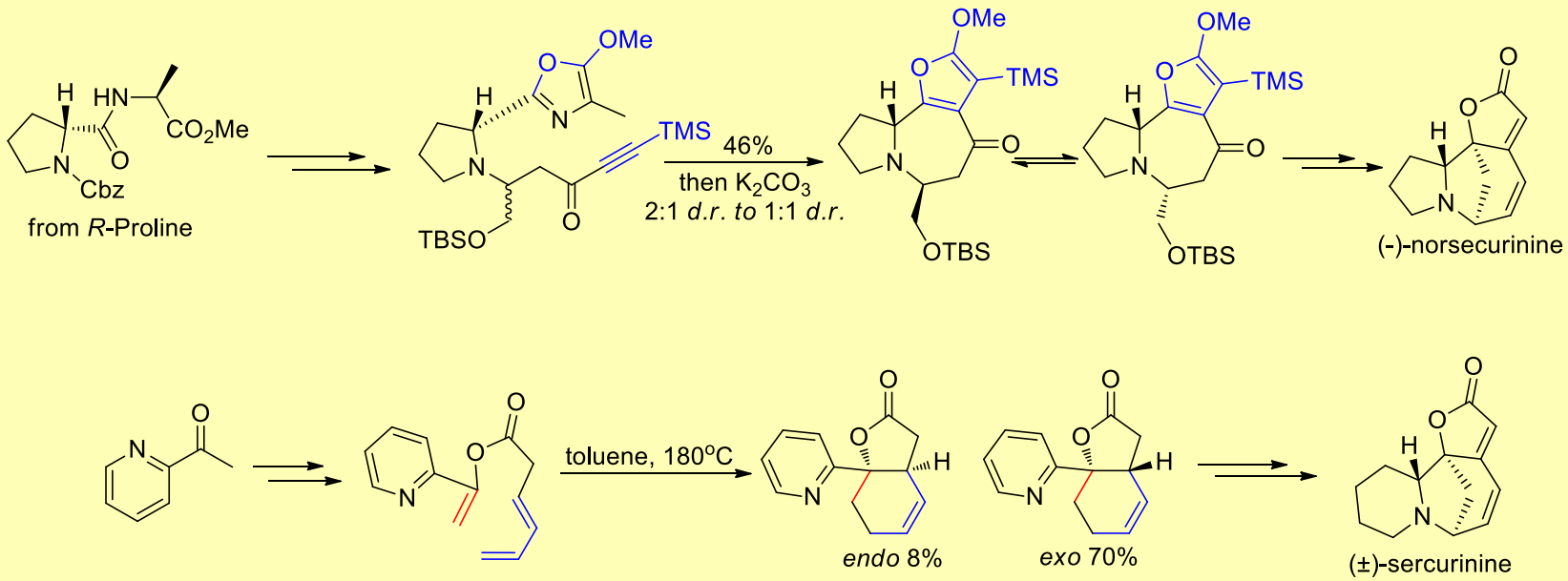
Diels-Alder Routes



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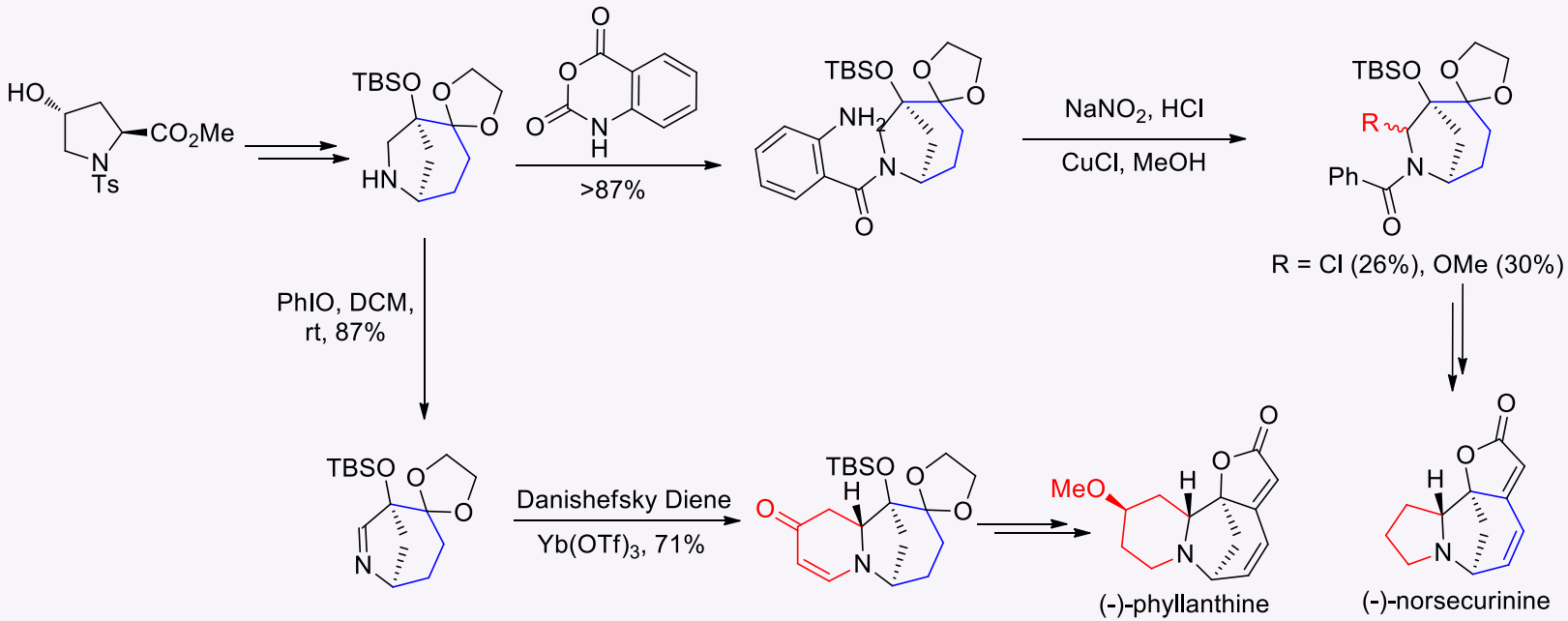
Weinreb's Synthesis of (-)-norsecurinine



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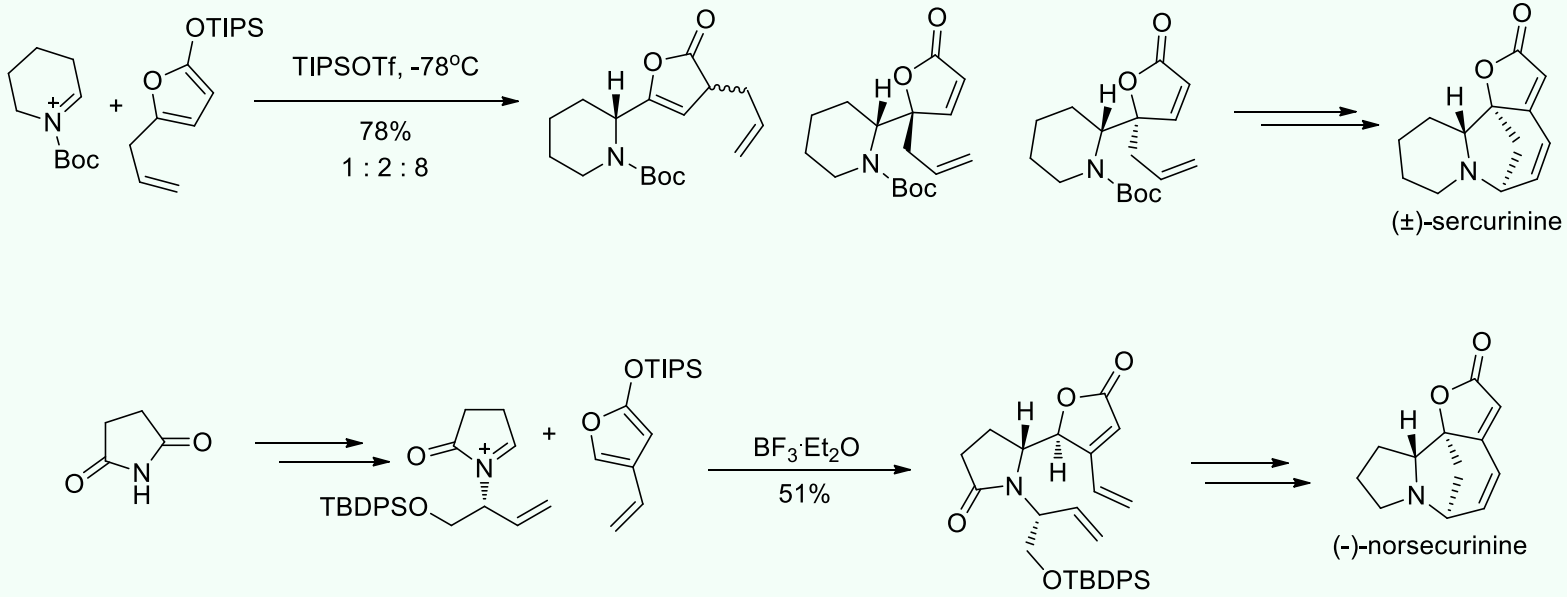
Vinylogous Mannich Reaction Route



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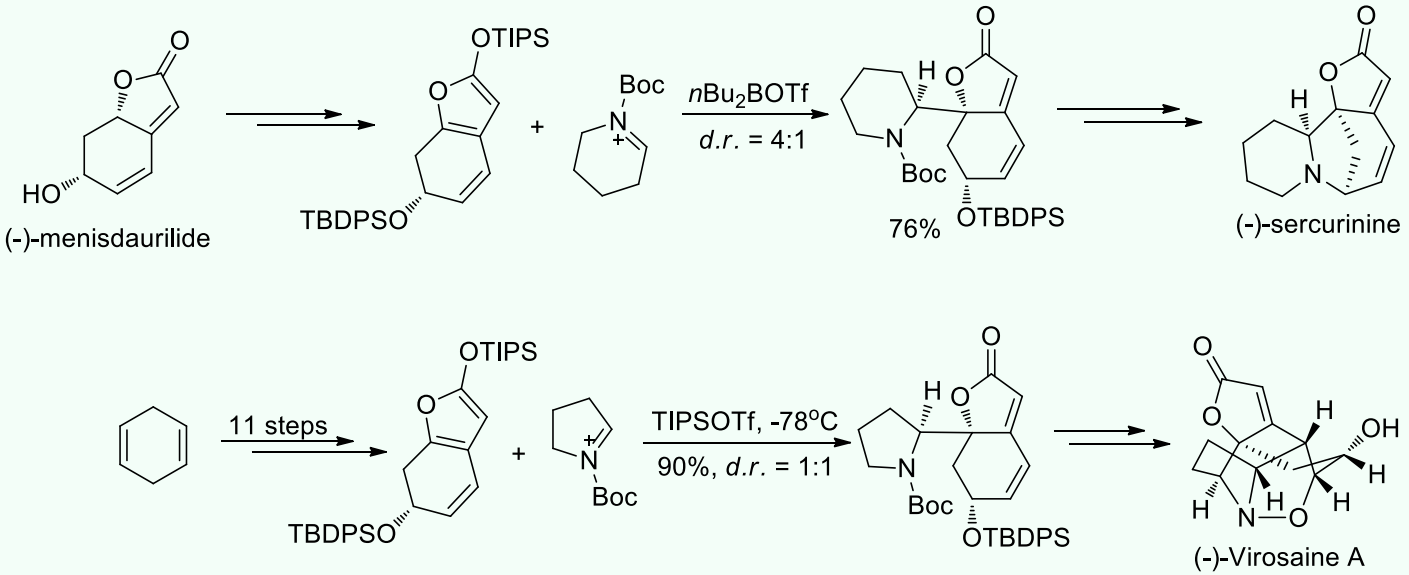
Vinylogous Mannich Reaction Route



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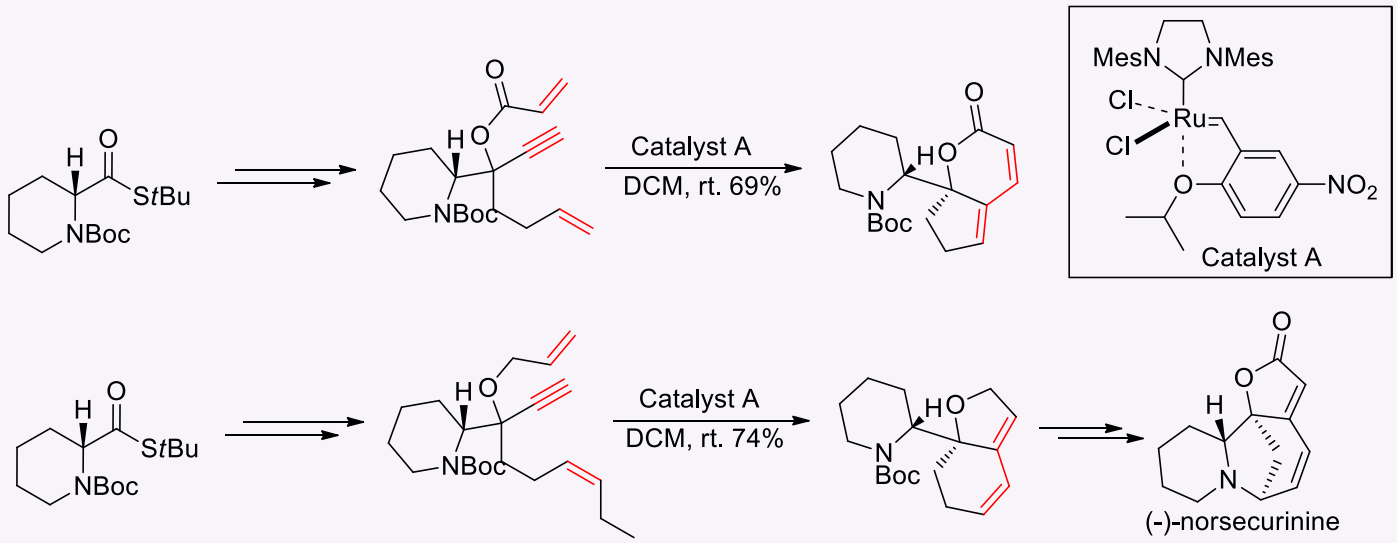
Tandem RCM Routes



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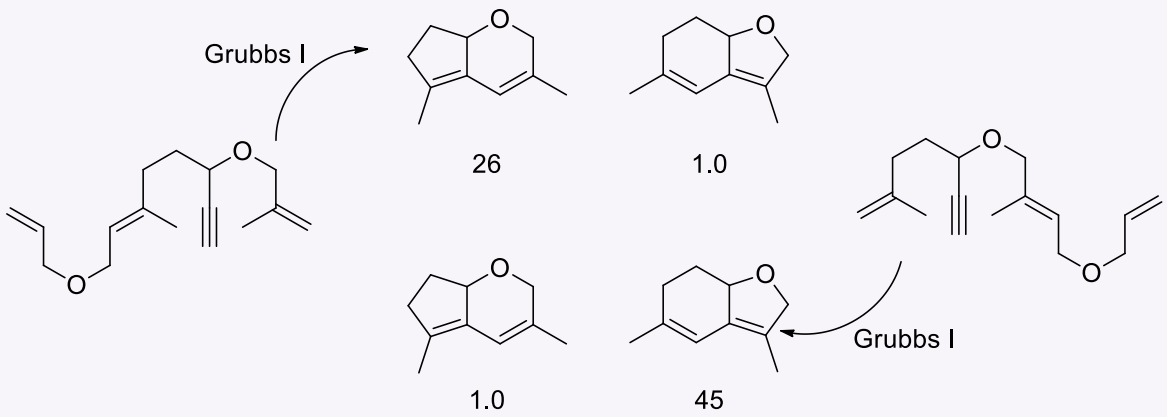
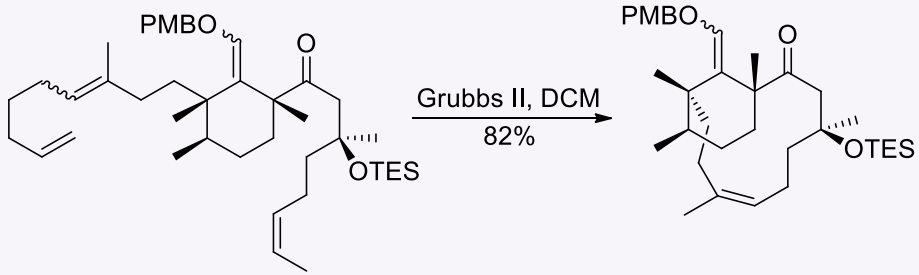
Relay RCM Strategy





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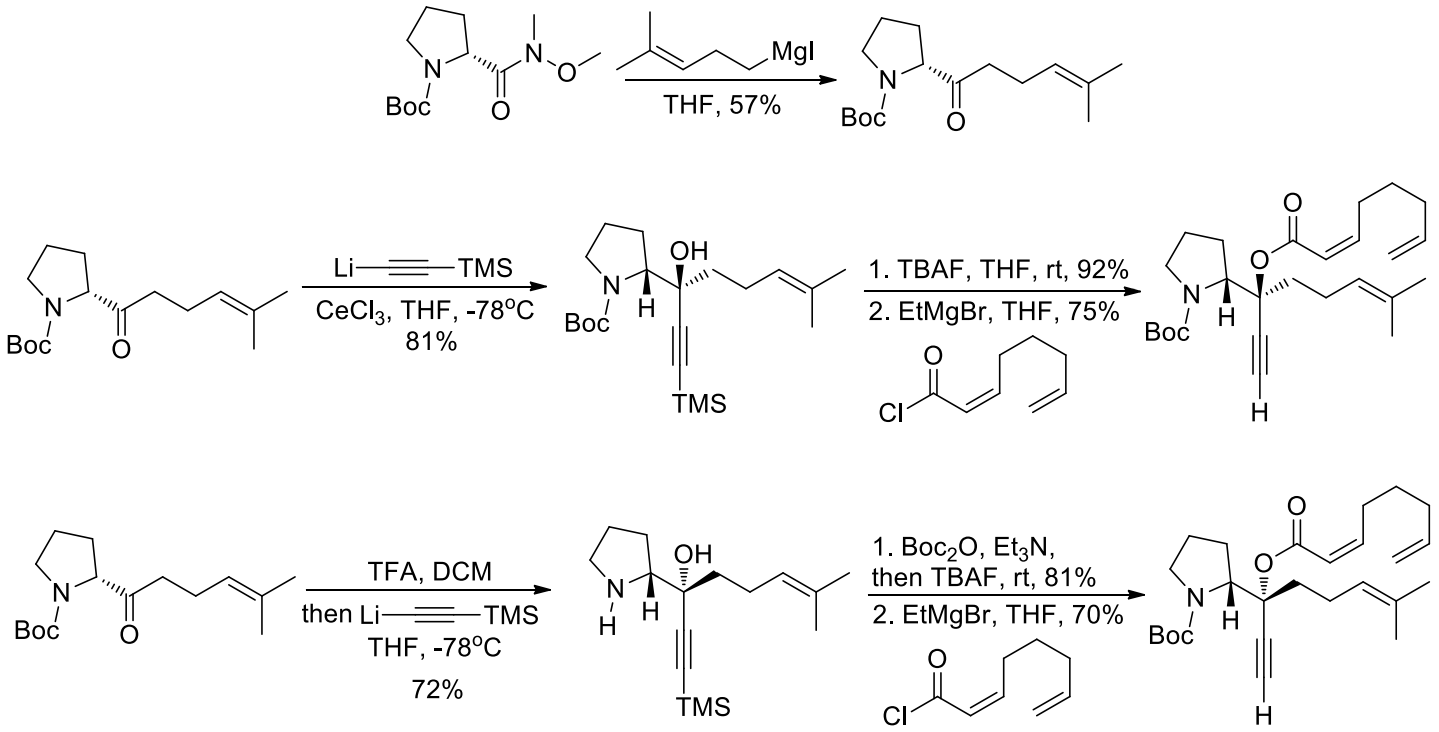
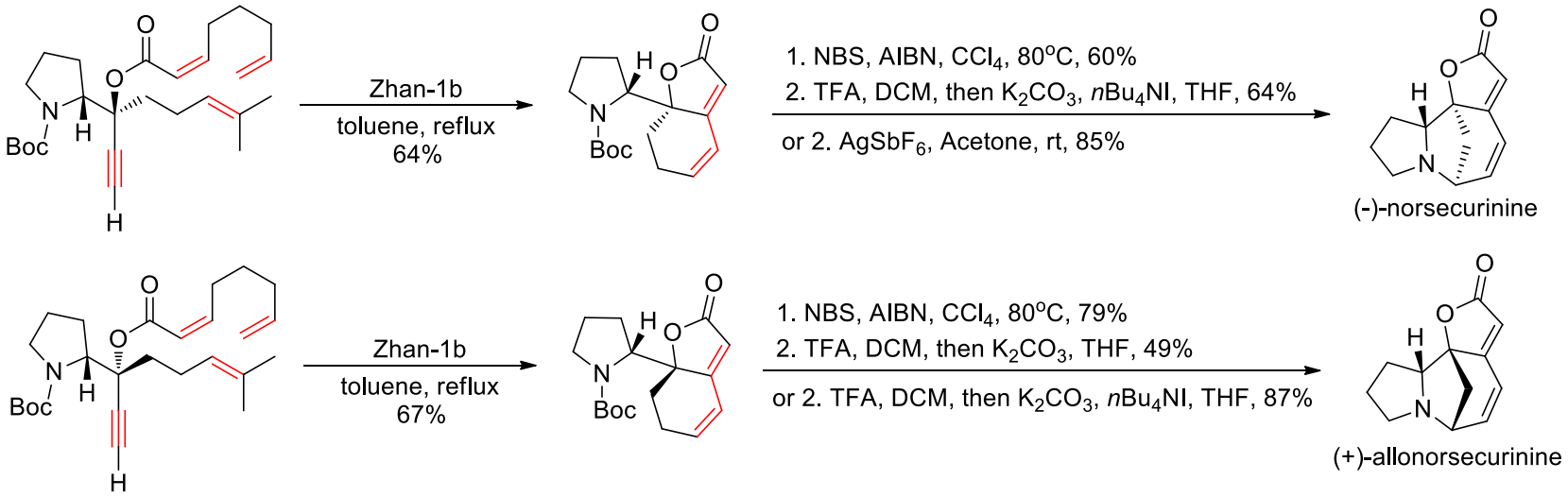
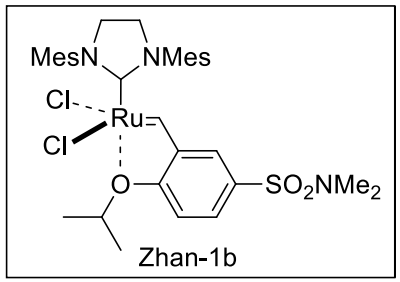
Synthesis of (-)-Norsecurinine and (+)-Allonorsecurinine



1. Wei, H., Qiao, C., Liu, G., Yang, Z. and Li, C.-c. *Angew. Chem. Int. Ed.*, 2013, ***52***: 620–624.

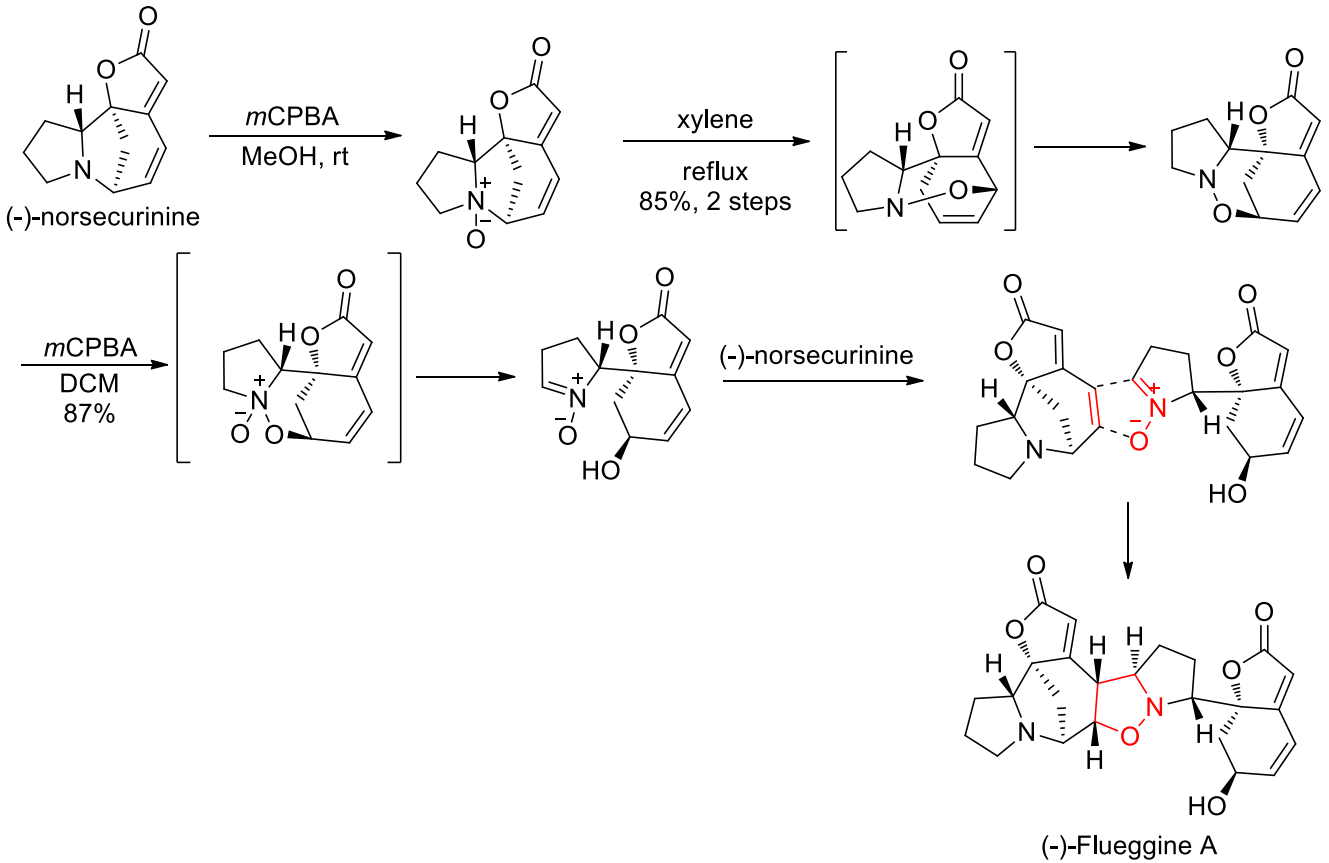
Synthesis of (-)-Norsecurinine and (+)-Allonorsecurinine





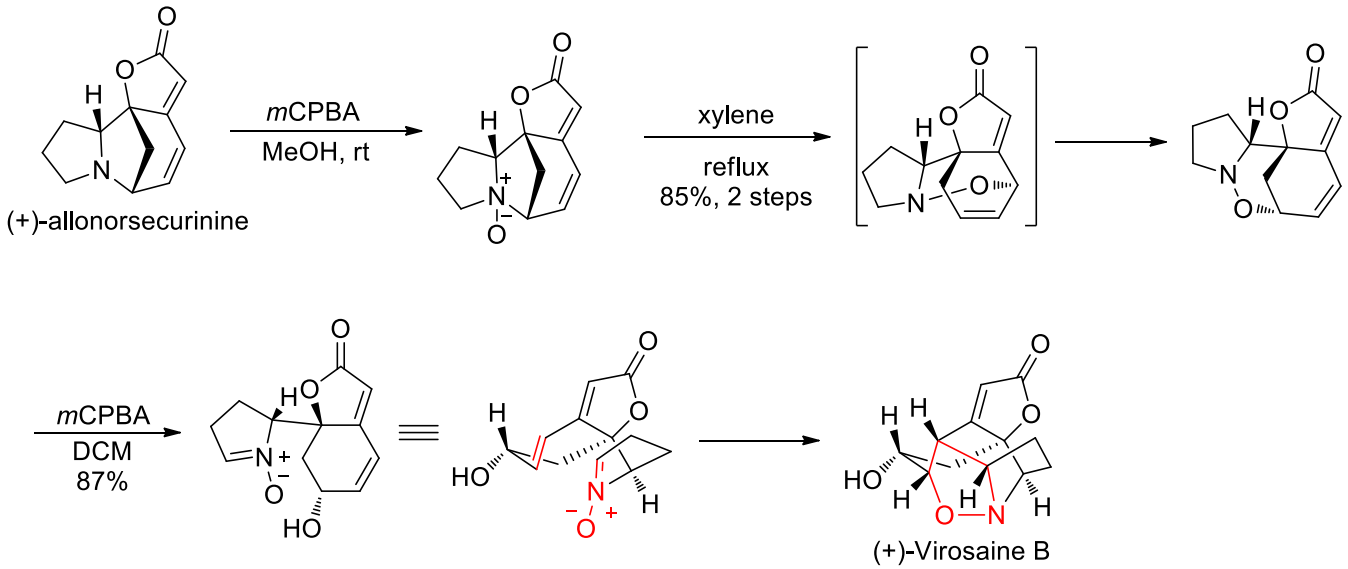
1. Wei, H., Qiao, C., Liu, G., Yang, Z. and Li, C.-c. *Angew. Chem. Int. Ed.*, 2013, ***52***: 620–624.

Synthesis of (-)-Flueggine A



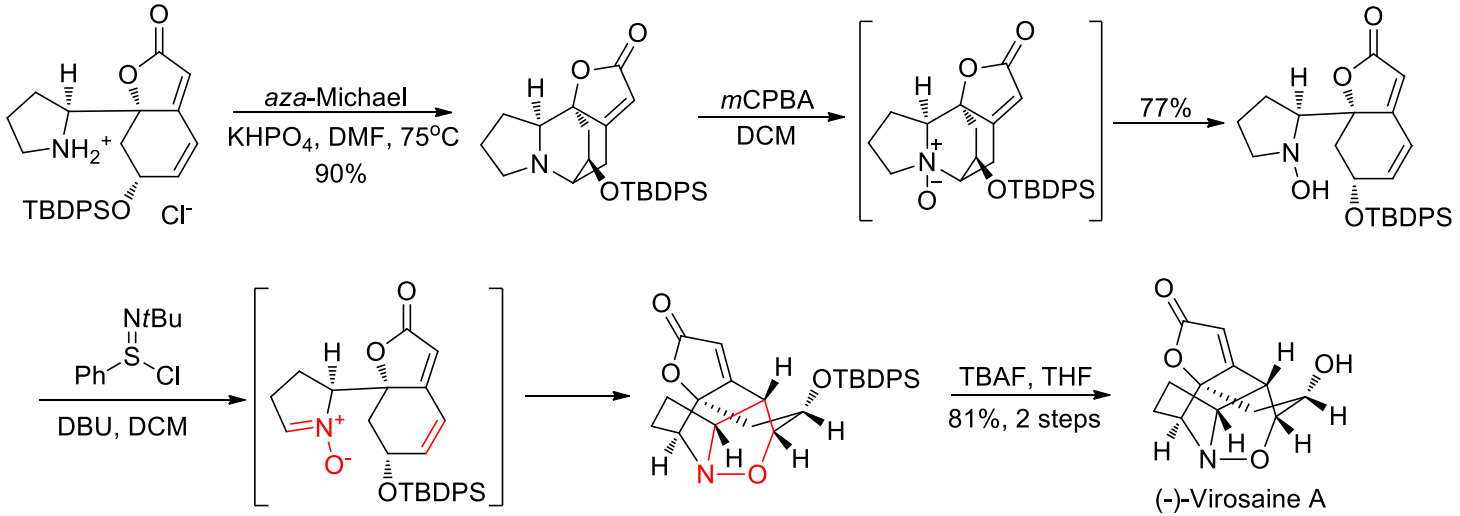
1. Wei, H., Qiao, C., Liu, G., Yang, Z. and Li, C.-c. *Angew. Chem. Int. Ed.*, 2013, ***52***: 620–624.

Synthesis of (+)-Virosaine B



1. Wei, H., Qiao, C., Liu, G., Yang, Z. and Li, C.-c. *Angew. Chem. Int. Ed.*, 2013, ***52***: 620–624.

Synthesis of (-)-Virosaine A



1. H. Miyatake-Ondozabal, L. M. Bannwart and K. Gademann. *Chem. Commun.*, 2013, ***49***, 1921

Summary

- 5.92% overall yield for (-)-Flueggine A
- 6.68% overall yield for (+)-Virosaine B
- Starting from commercially available Weinreb amide.
- Tandem RRCMs strategy and 1,3-dipolar cycloadditions as two key steps.