五、一些形成C–C键的基本反应
（四）烯基化反应

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生命有机化学国家重点实验室

2016年12月5日

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二、基础知识

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有机反应的热力学和动力学

构象对反应活性的影响

立体电子效应

三、氧化态的调整

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烯烃、羰基化合物和其他化合物的还原

四、C-X键形成反应

五、一些形成C–C键的基本反应

烯醇和烯醇负离子化学

有机锂、镁和铜试剂的制备和反应

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烯基化反应

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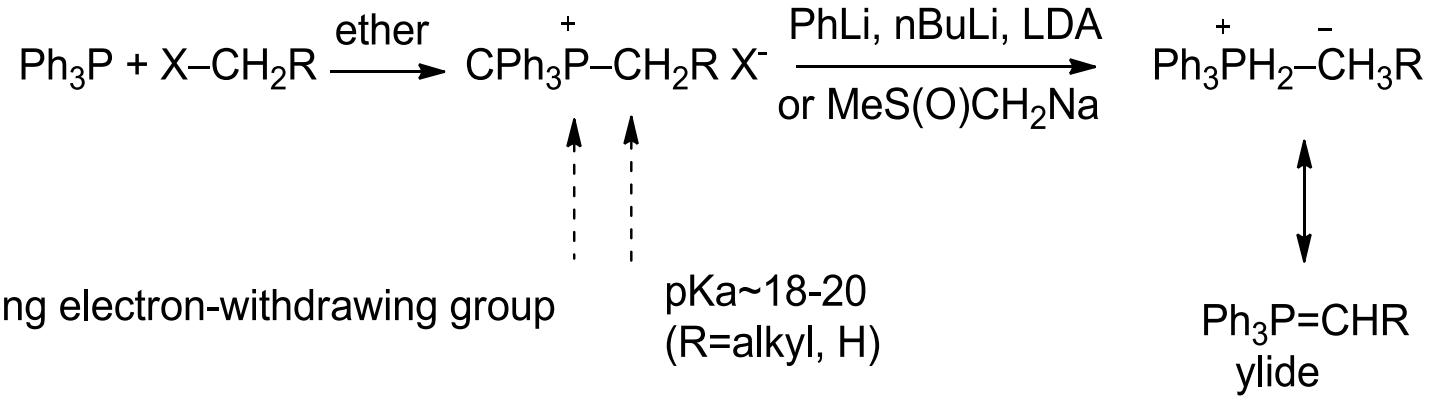
电环化反应

sigmatropic重排

七、阳离子参与的C–C键形成反应

Wittig反应的基本常识

Formation of Ylides

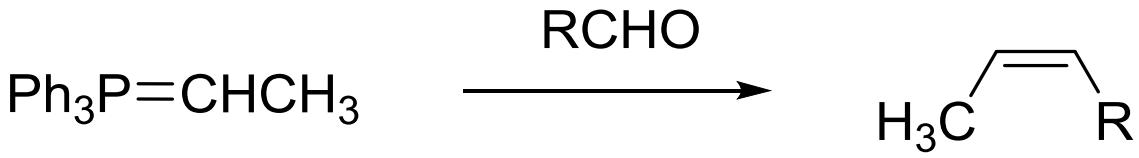


-Unstablized ylides are sensitive to H_2O, O_2

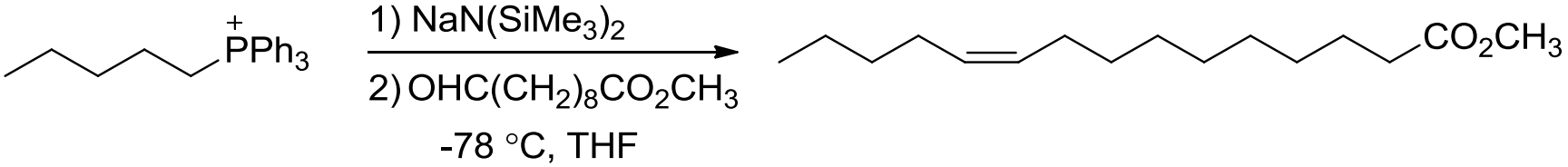
Wittig, Schöllkopf *Chem. Ber.* **1954**, *87*, 1318.

Wittig反应的基本常识 ：非稳定ylide的顺反选择性

Stereoselectivity of the Wittig Reaction

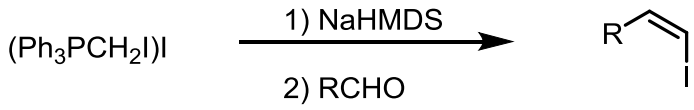


cis olefin from nonstabilized ylides

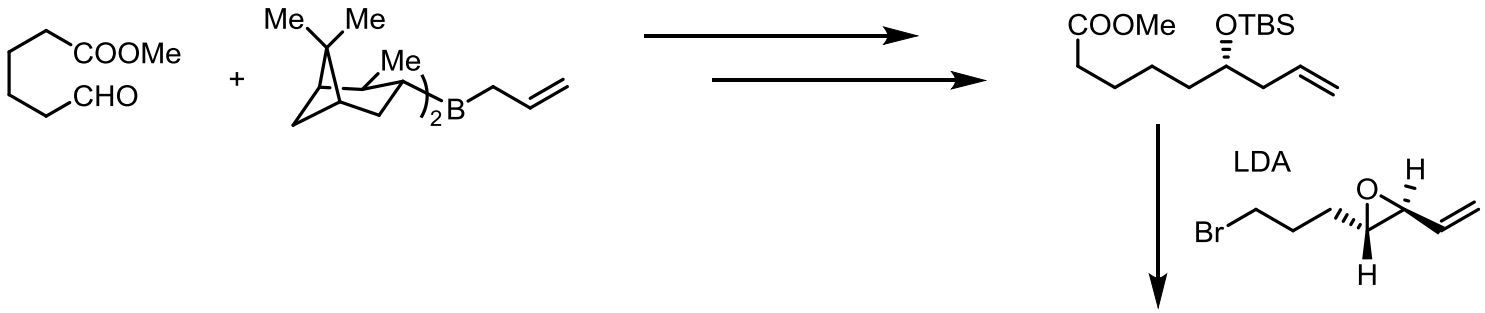


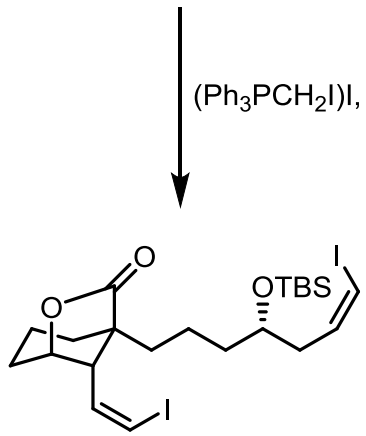
Besterman *Chem. Ber.* **1976**, *109*, 1694.

Wittig反应: 卤代烯烃的合成/Stork-Zhao olefination

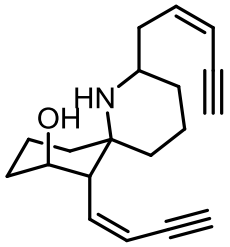


Stork, G., Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 2173.





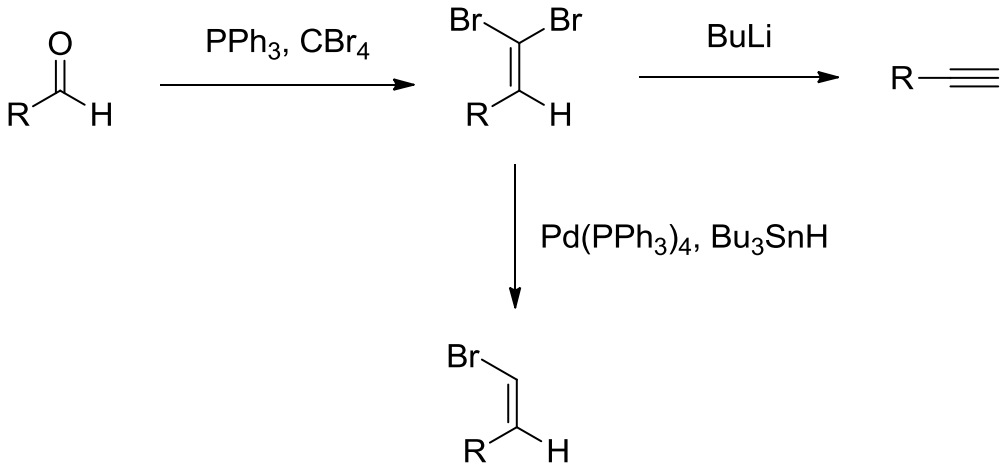
Stork, G., Zhao, K. *J. Am. Chem. Soc.* **1990**, *112*, 5876.



histrionicotoxin

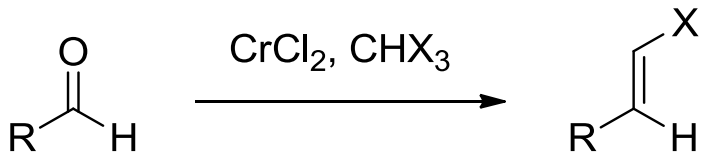
Wittig反应：卤代烯烃的合成

Corey-Fuchs reaction



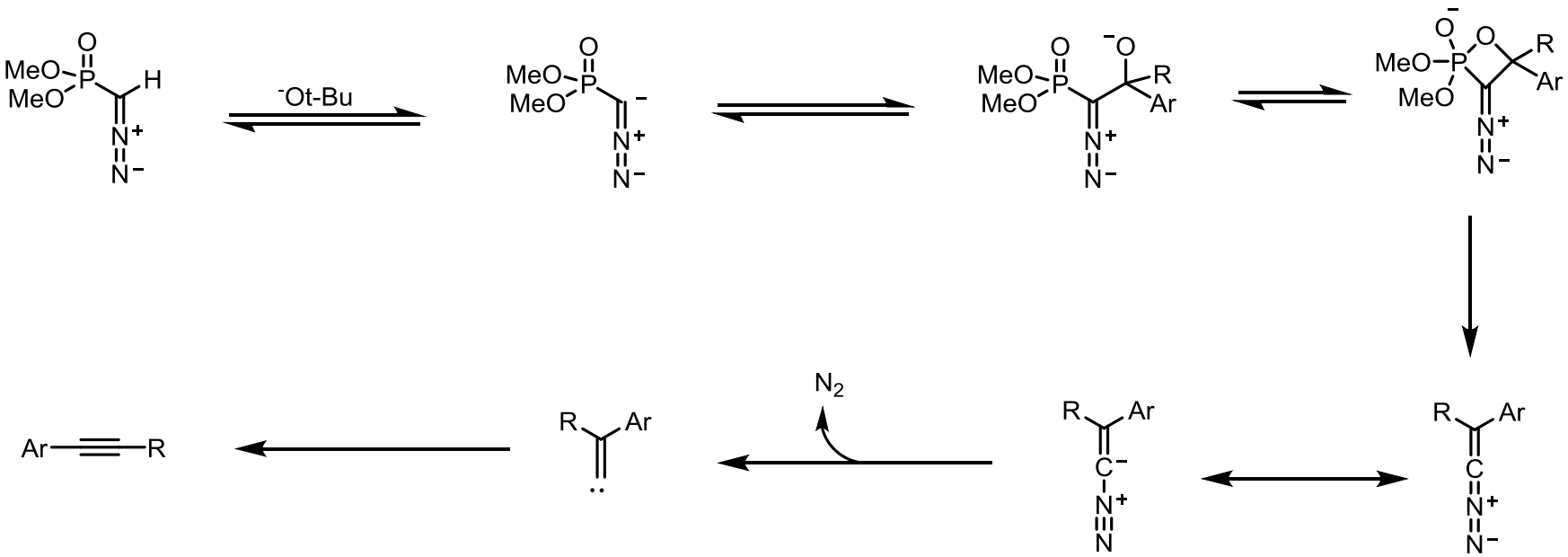
Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13*, 3769.

Takai olefination

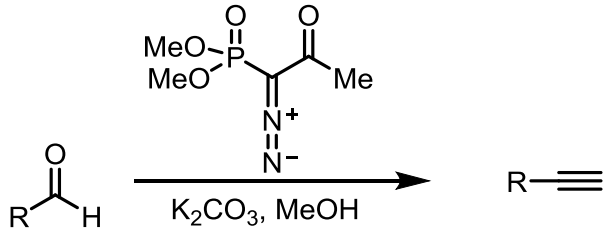


Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408.

Seyferth–Gilbert homologation反应



Bestmann modification

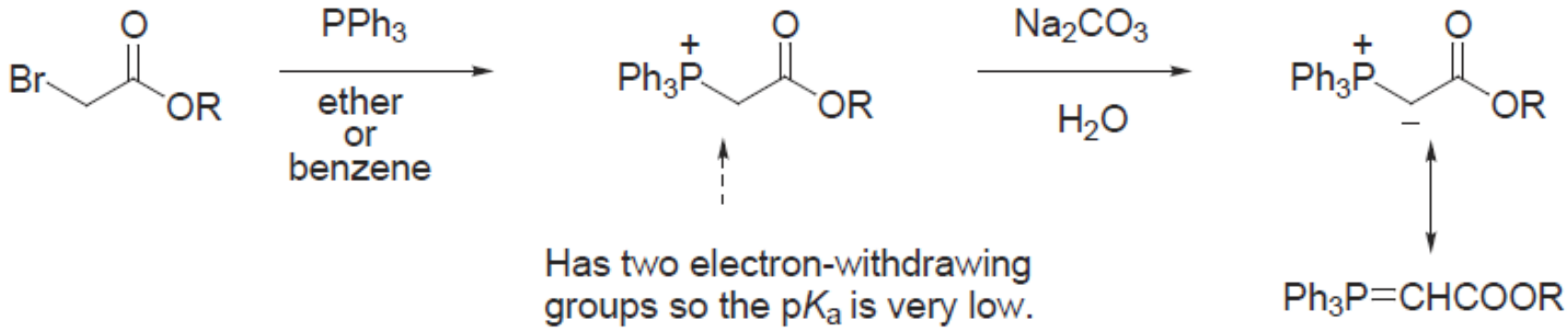


D. Seyferth, R. S. Marmor and P. Hilbert *J. Org. Chem*. **1971**, *36*, 1379.

S. Müller, B. Liepold, G. Roth and H. J. Bestmann *Synlett* **1996**, 521.

Wittig反应的基本常识：稳定ylide

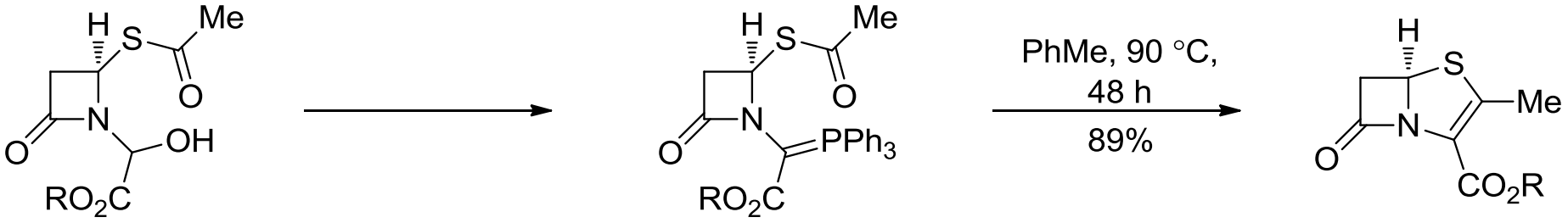
Stabilized Ylides



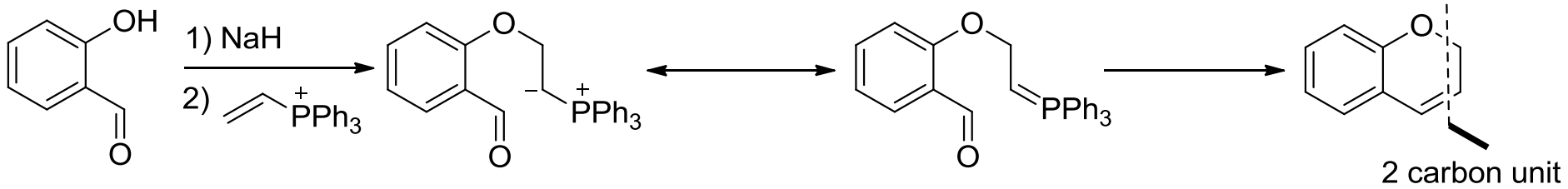
Has two electron-withdrawing groups so the pK_a is very low.

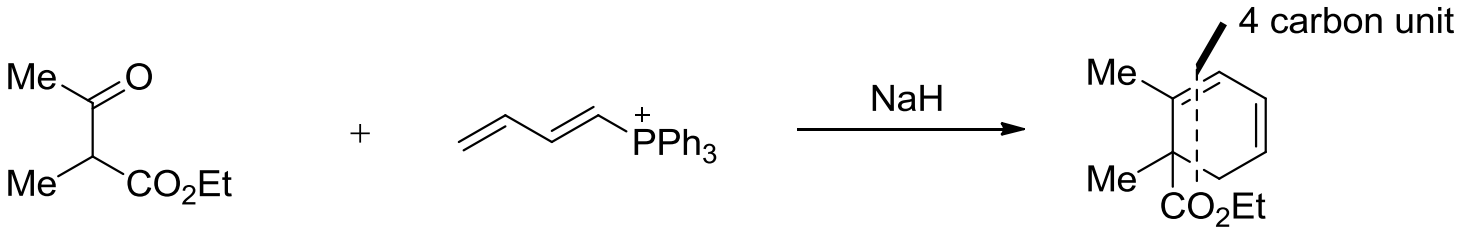
- Stabilized ylides are solid; stable to storage, not particularly sensitive to moisture, and can even be purified by chromatography.
- Because they are stabilized, they are much less reactive than alkyl ylides. They react well with aldehydes, but only slowly with ketones.
- The first step, involving the addition to the aldehyde, is slow and reversible with stabilized ylides.

Wittig反应的一些变化



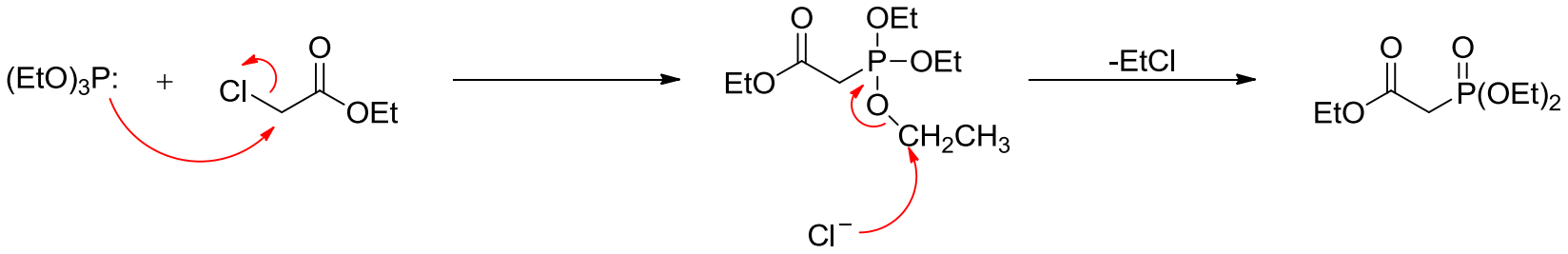
Woodward *J. Am. Chem. Soc.* **1979**, *101*, 6301.



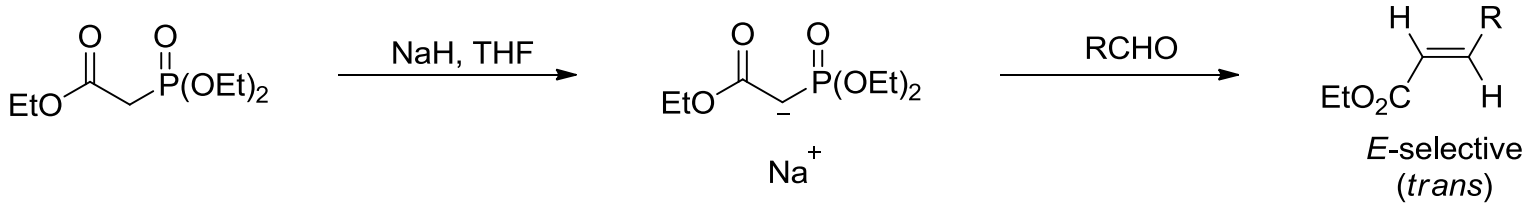


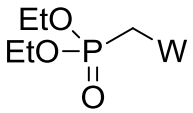
Horner-Wadsworth-Emmons反应

Arbuzov (Michaelis–Arbuzov) Reaction: Preparation of Phosphonate Esters



Arbuzov *Pure Appl. Chem.* **1964**, *9*, 307.





W = CN, COOR, C(O)R, CHO, SO_2Ph, Ph
W not = alkyl, H

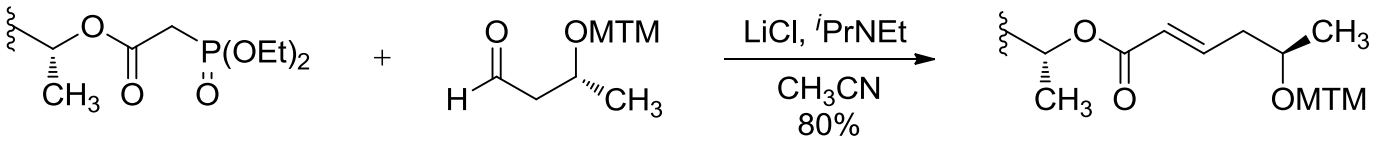
Wadsworth, Emmons *J. Am. Chem. Soc.* **1961**, *83*, 1733.

Horner-Wadsworth-Emmons反应：改进

Masamune-Roush conditions

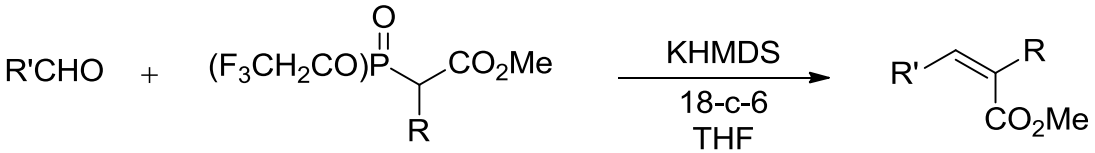
- LiCl/tertiary amines (DBU, $^{i}Pr_2NEt$, Et_3N)

Masamune, Roush *Tetrahedron Lett*. **1984**, *25*, 2183.
Can substitute for conventional conditions and is especially good for base sensitive substrates (epimerization, elimination).



subject to β-elimination

Still-Gennari Olefination

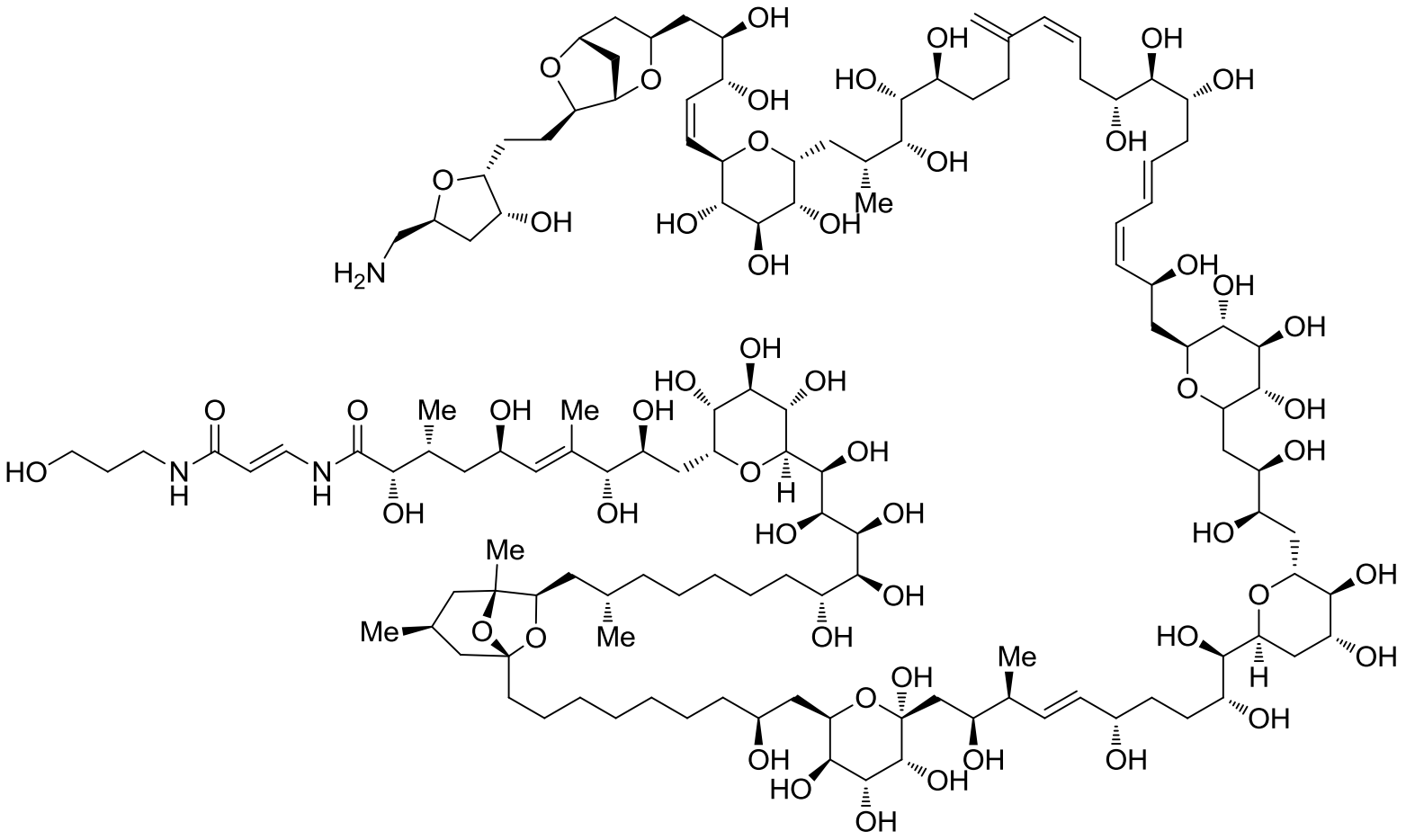


R = H, Me

Z : *E* > 10 : 1

Still *Tetrahedron Lett*. **1983**, *24*, 4405.

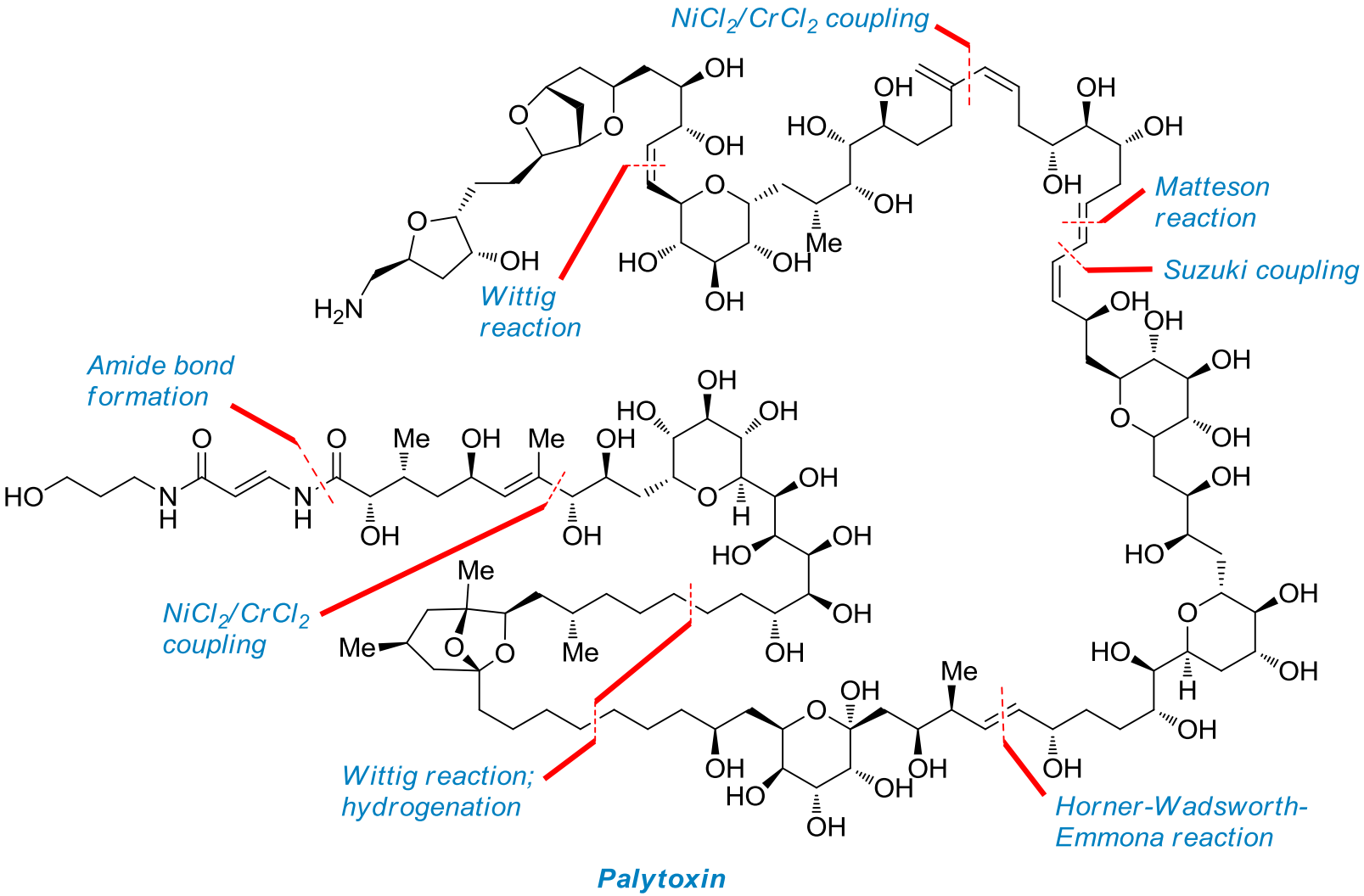
Horner-Wadsworth-Emmons反应：改进



Palytoxin

Yoshito Kishi, et al. 1994

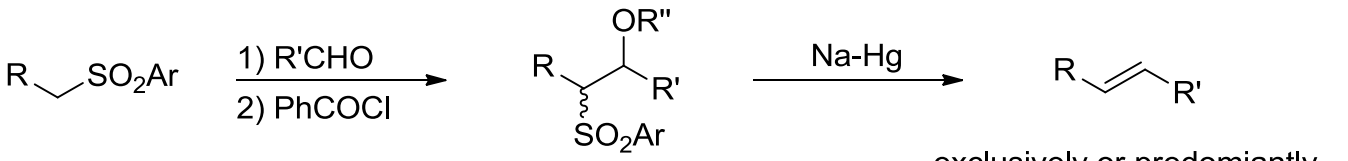
Horner-Wadsworth-Emmons反应：改进



Palytoxin

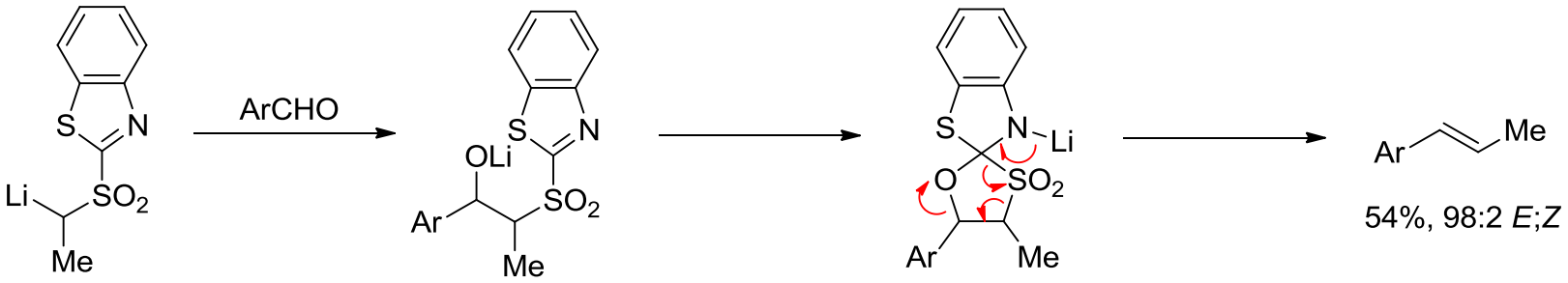
Yoshito Kishi, et al. 1994

Julia Olefination



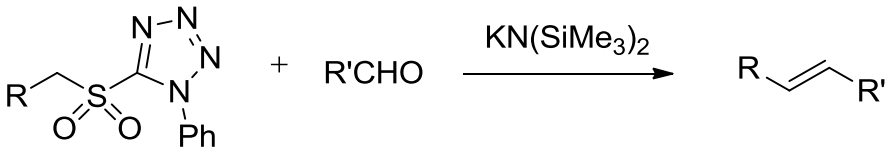
R" = Ms, Ts, Ac, COPh

exclusively or predomiantly
the more stable *trans* isomer



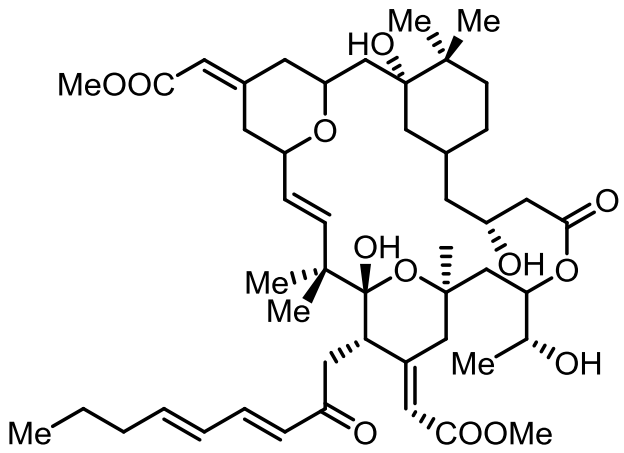
54%, 98:2 *E*;*Z*

Julia *Bull. Soc. Chim., Fr.* **1993**, *130*, 336.

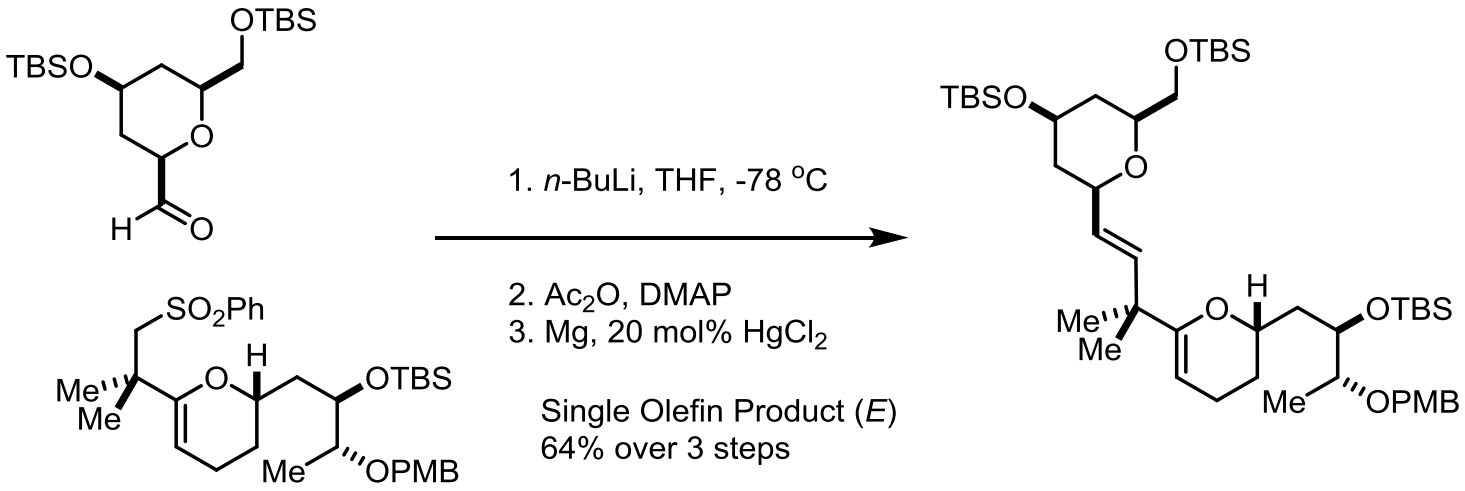


Paul R. Blakemore, William J. Cole, Philip J. Kocieński, Andrew Morley *Synlett* **1998**, 26.

Julia Olefination: Bryostatin 2 Synthesis

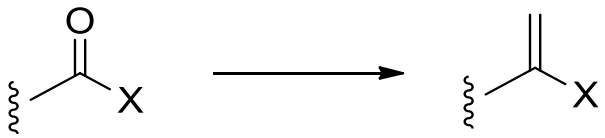


bryostatin

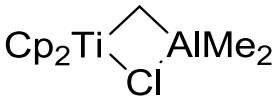


D. A. Evans, P. H. Carter, E. M. Carreira, A. B. Charette, J. A. Prunet, M. Lartens *J. Am. Chem. Soc.* **1999**, *121*, 7540.

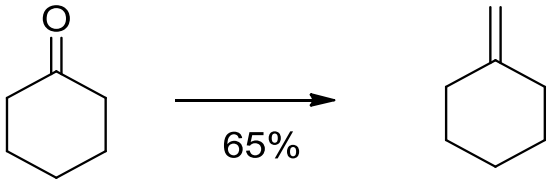
Tebbe Reaction and Related Reactions

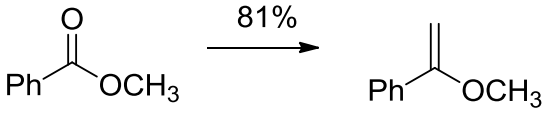


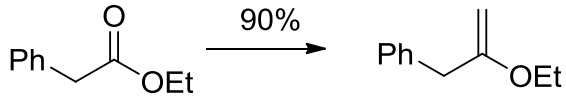
X= H, R, OR, NR_2

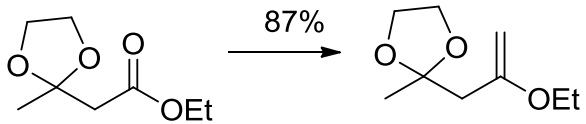


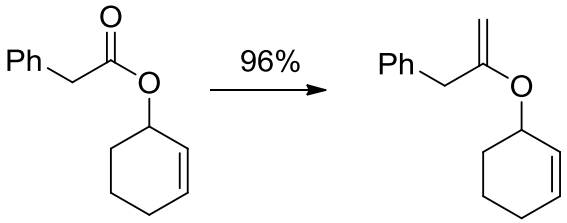
Tebbe reagent

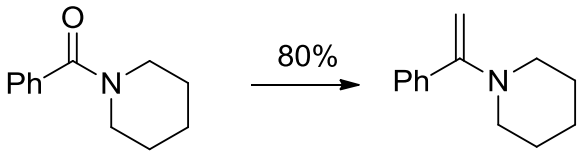






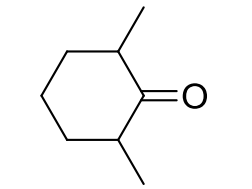


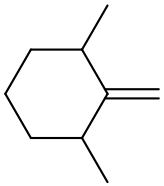




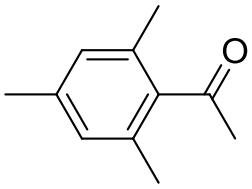
Tebbe VS Wittig

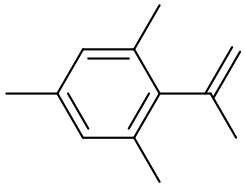
Tebbe vs Witting



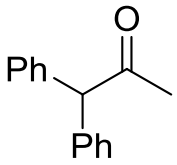


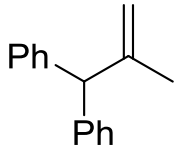
Tebbe	Witting
97%	89%





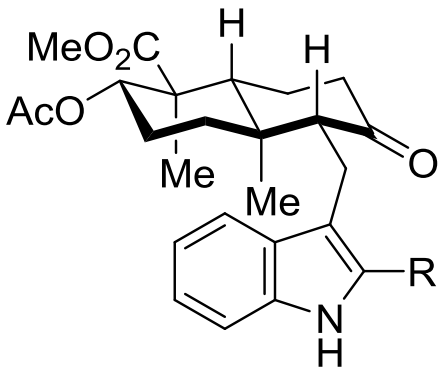
Tebbe	Witting
77%	4%



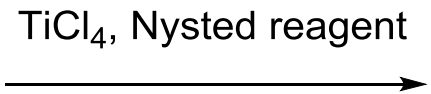


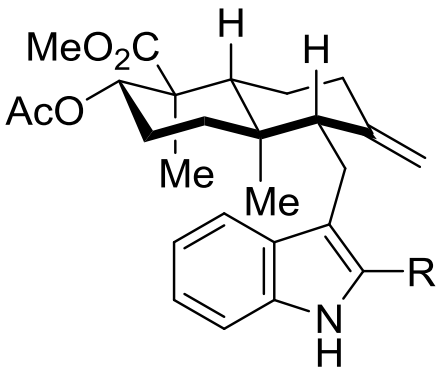
Tebbe	Witting
63%	38%

Nysted Reaction

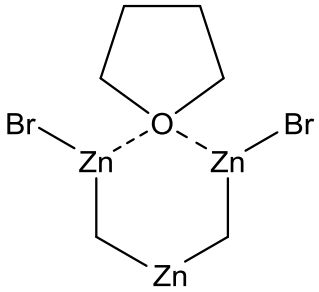


1: R = H
2: R = CO_2Me





3: R = H, 64 %
4: R = CO_2Me, 78 %

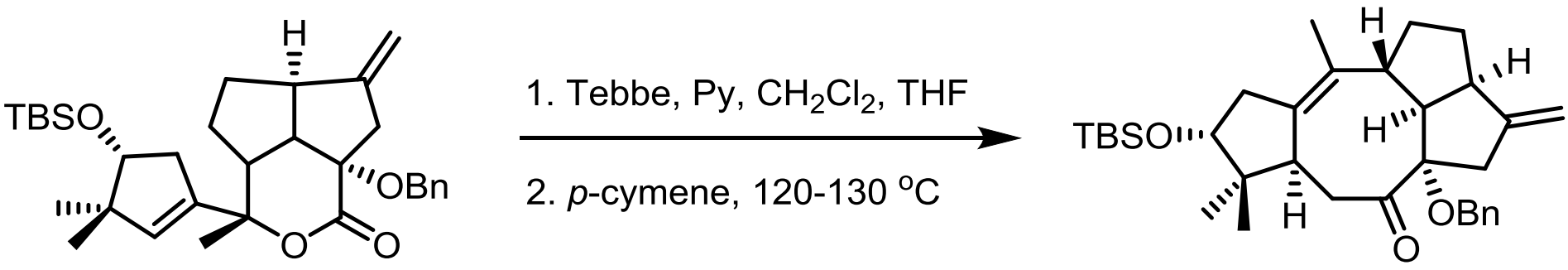


Nysted reagent

Y. Sun, P. Chen, D. Zhang, M. Baunach, C. Hertweck, A. Li,
Angew. Chem. Int. Ed. **2014**, *53*, 9012.

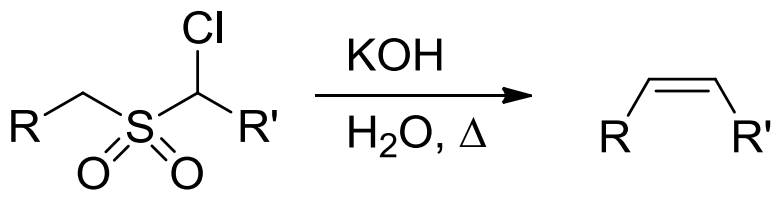
L. N. Nysted, US Patent, **1975**, 3 865 848.
"Nysted Reagent." Comprehensive Organic Name Reactions and Reagents. 2010 John Wiley and Sons, Inc.
W. Tochtermann, S. Bruhn, M. Meints, C.Wolff, E.-M. Peters, K. Peters, H. G. von Schnering,
Tetrahedron **1995**, *51*, 1623.

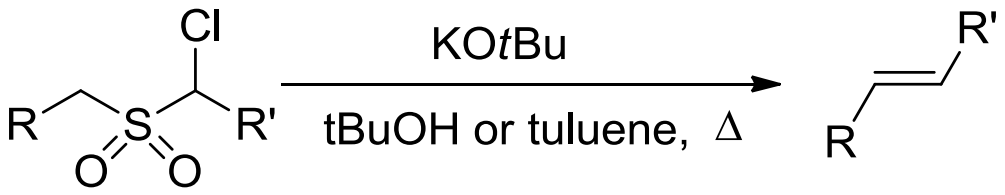
Tebbe-Claisen Cascade



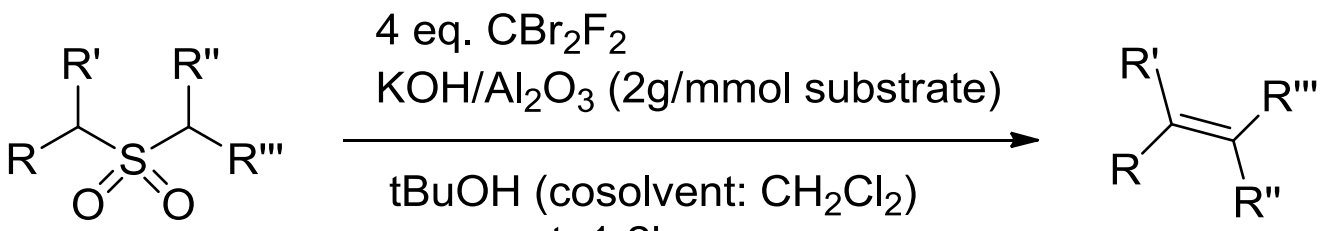
L. A. Paquette, et. al. *J. Am. Chem. Soc*. **1996**, *118*, 727.

Tebbe Cascade





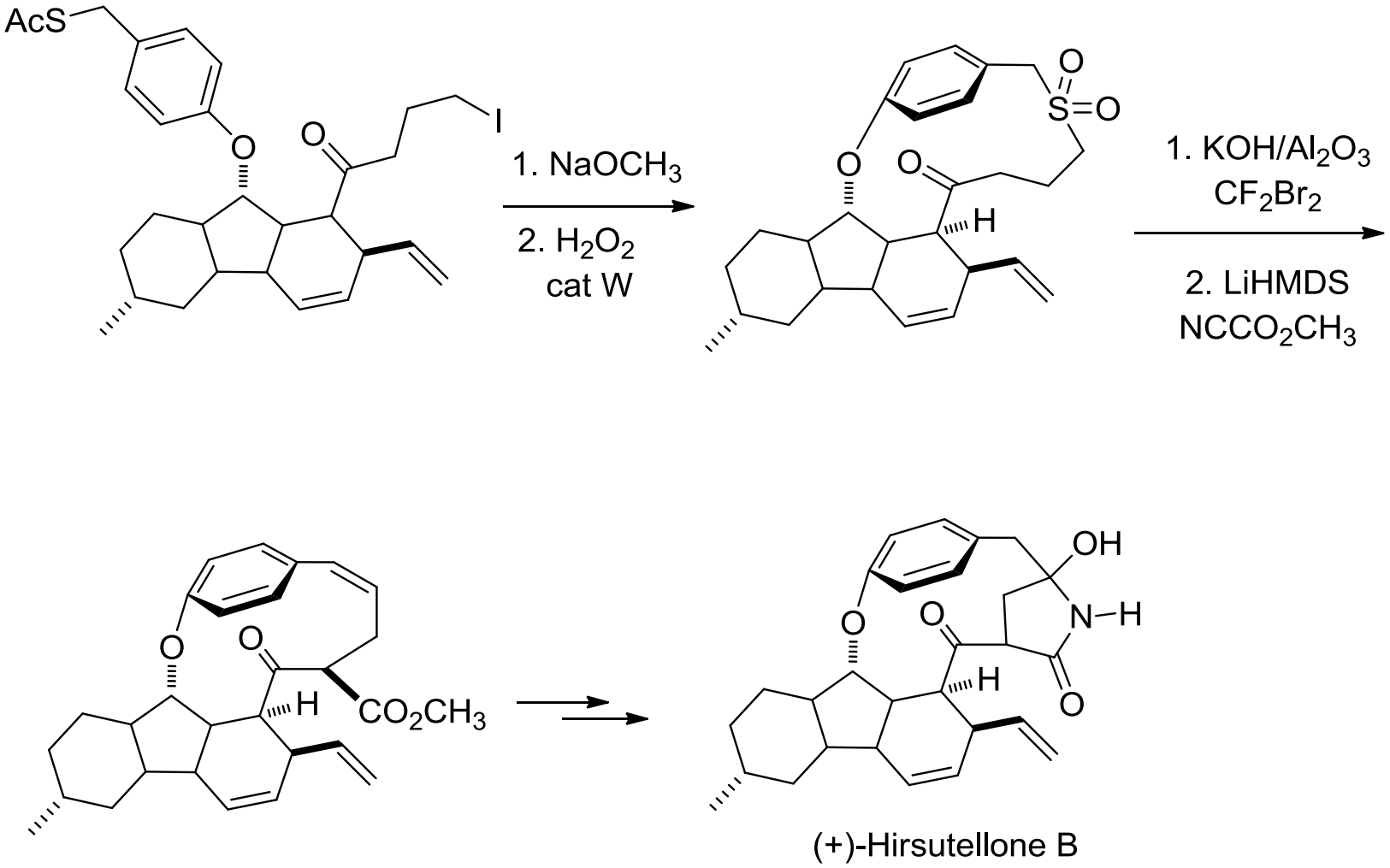
Chan Modification



R, R''': alkyl, Ar
R', R'': H, alkyl

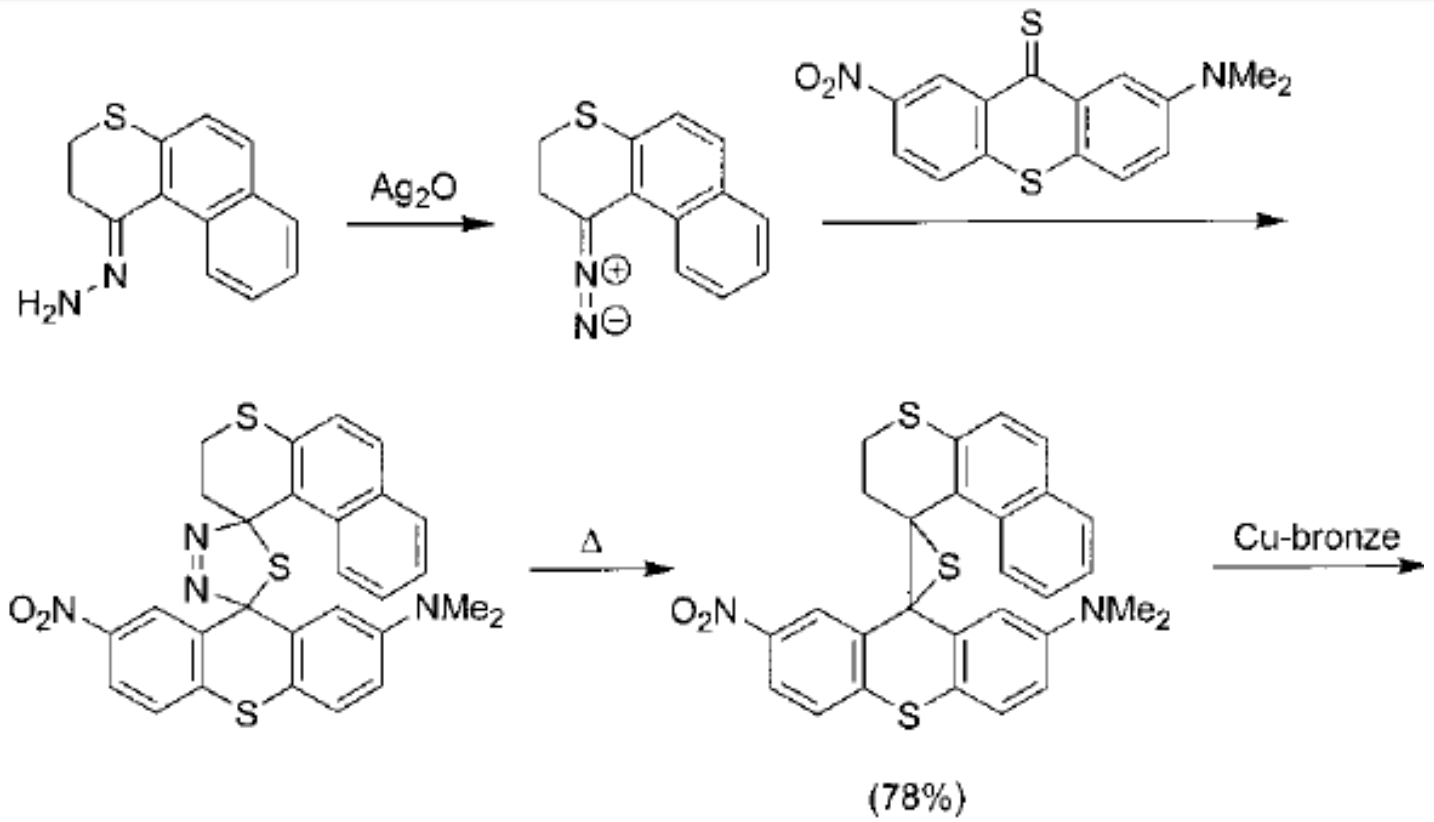
T. L. Chan, S. Fong, Y. Li, T. O. Man, C. D. Poon. *J. Chem. Soc., Commun*., **1994**, 1771.

Ramberg–Backlund reaction: Hirsutellone B Synthesis

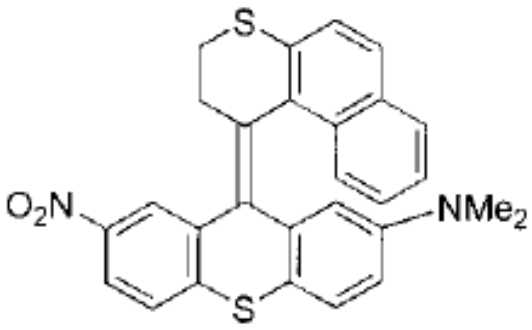


K. C. Nicolaou, et al. *Angew. Chem. Int. Ed*. **2009**, 49, 6870.

Barton–Kellogg reaction：四取代双键的构建

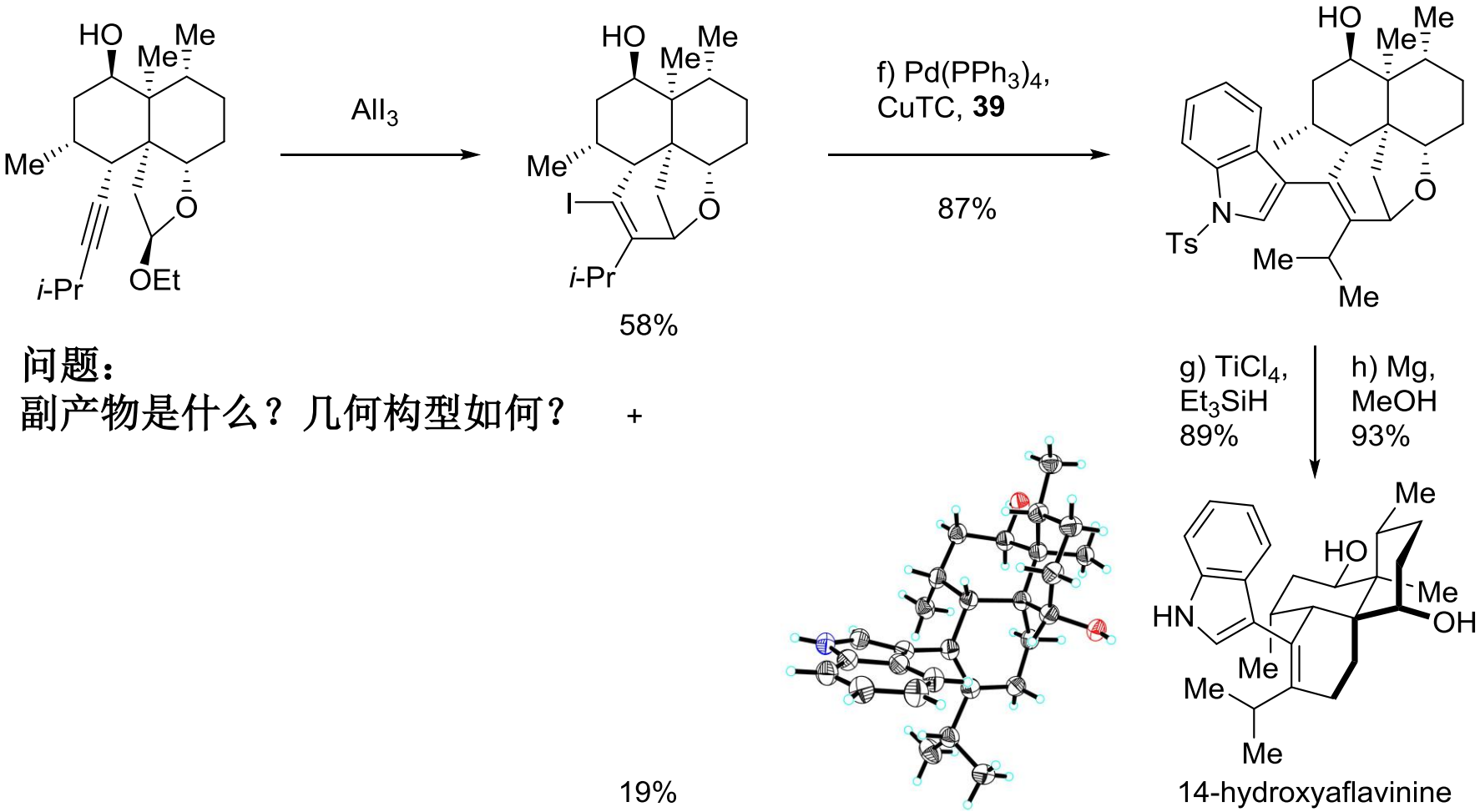


(78%)



2 (80%)

Alkyne Prins reaction：四取代双键的构建

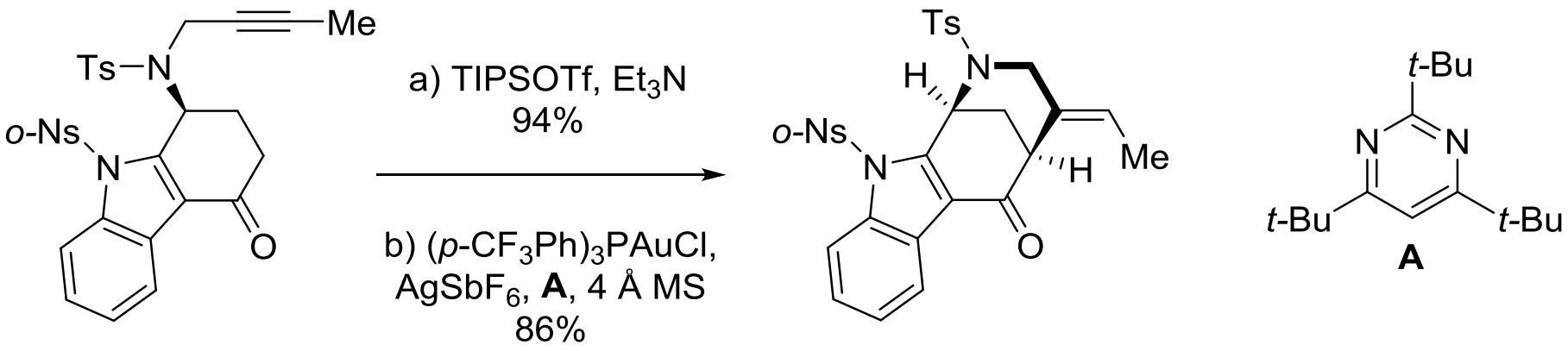


问题：
副产物是什么？几何构型如何？ +

19%

原始文献：H. Li, Q. Chen, Z. Lu, A. Li, *J. Am. Chem. Soc.* doi: 10.1021/jacs.6b10880.

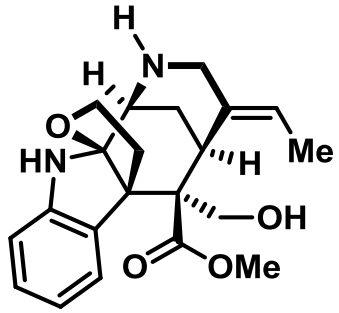
烯烃顺反几何构型的调控



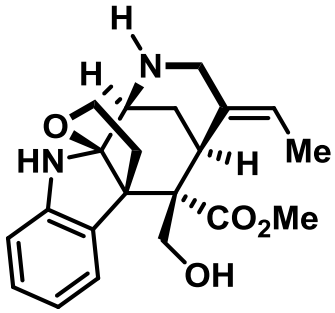
问题：

(1) A的作用是什么?

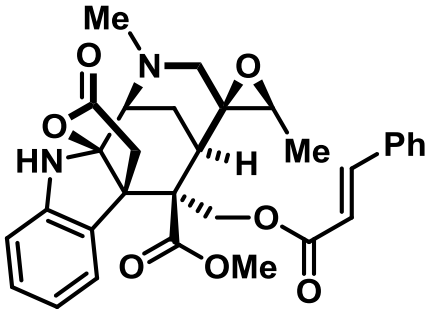
(2) 三取代双键的几何构型如何实现控制?



aspidodasicarpine



lonicerine



the proposed structure of lanciferine

原始文献：Y. Li, S. Zhu, J. Li, A. Li, *J. Am. Chem. Soc.* **2016**, *138*, 3982.