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

2018年11月26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
烯烃、醇和其他化合物的氧化
烯烃、羰基化合物和其他化合物的还原
四、C-X键形成反应
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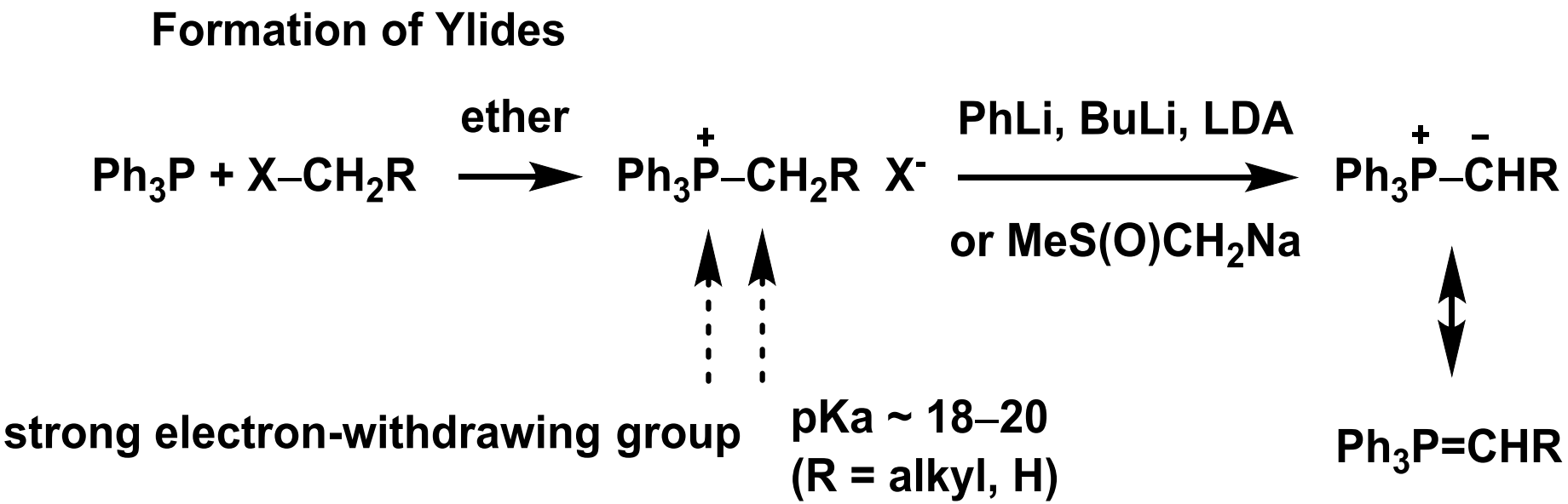
电环化反应
sigmatropic重排
七、阳离子参与的C–C键形成反应

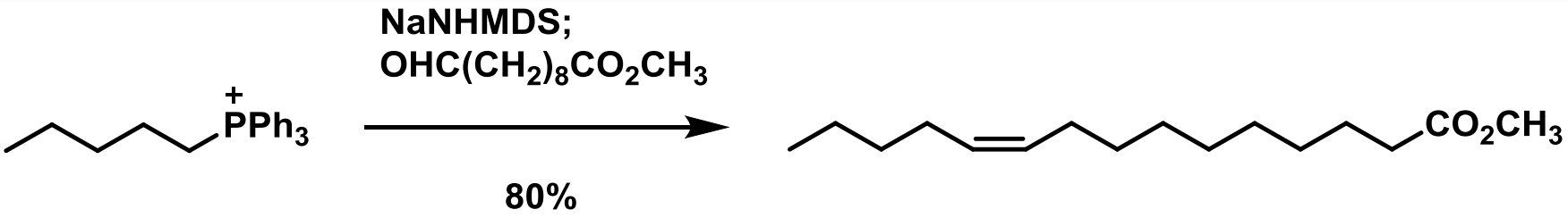
Wittig反应的中的非稳定ylide



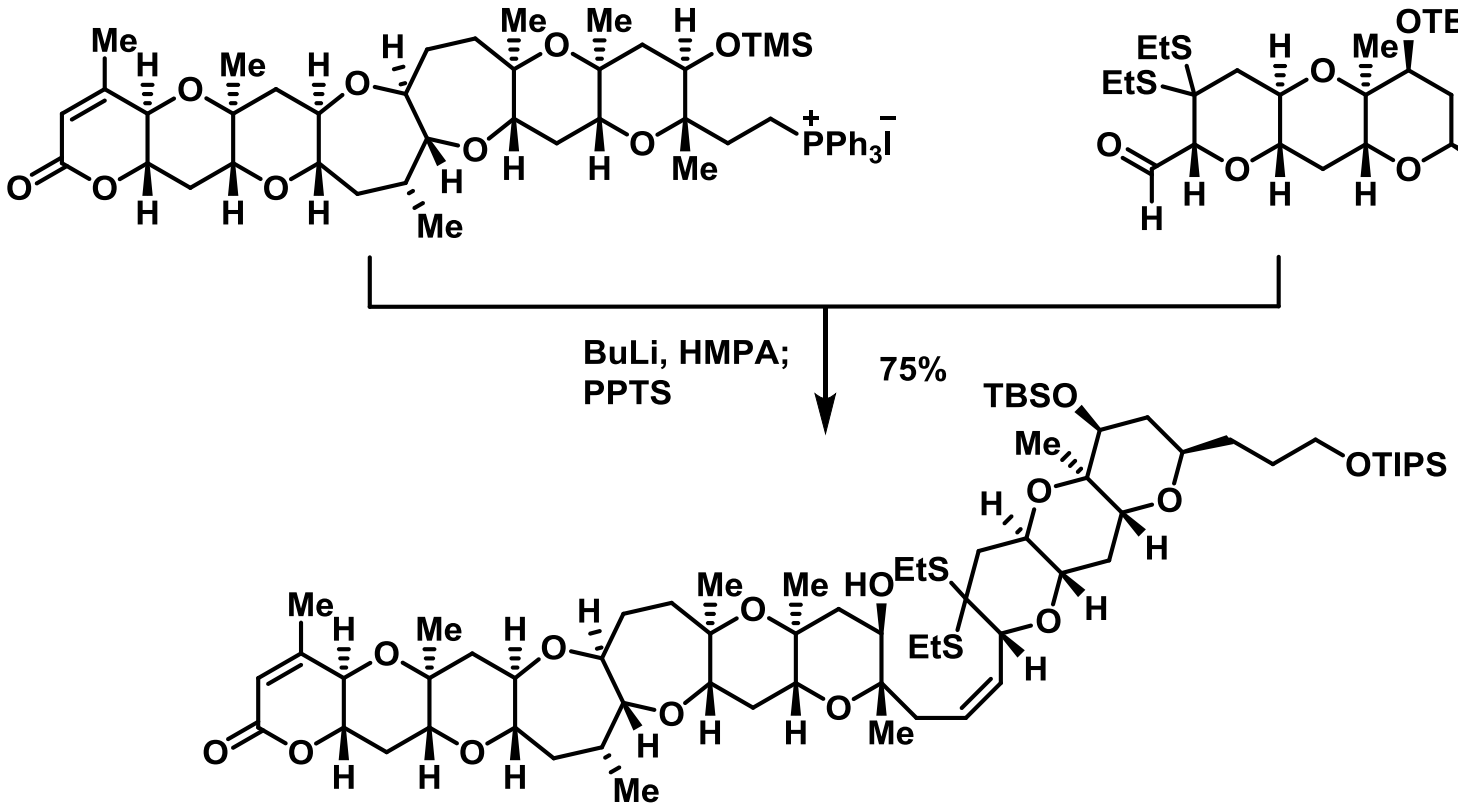
-Unstablized ylides are sensitive to H_2O, O_2

Wittig, et al. *Chem. Ber.* **1954**, *87*, 1318.

非稳定ylide烯基化产物的顺反选择性

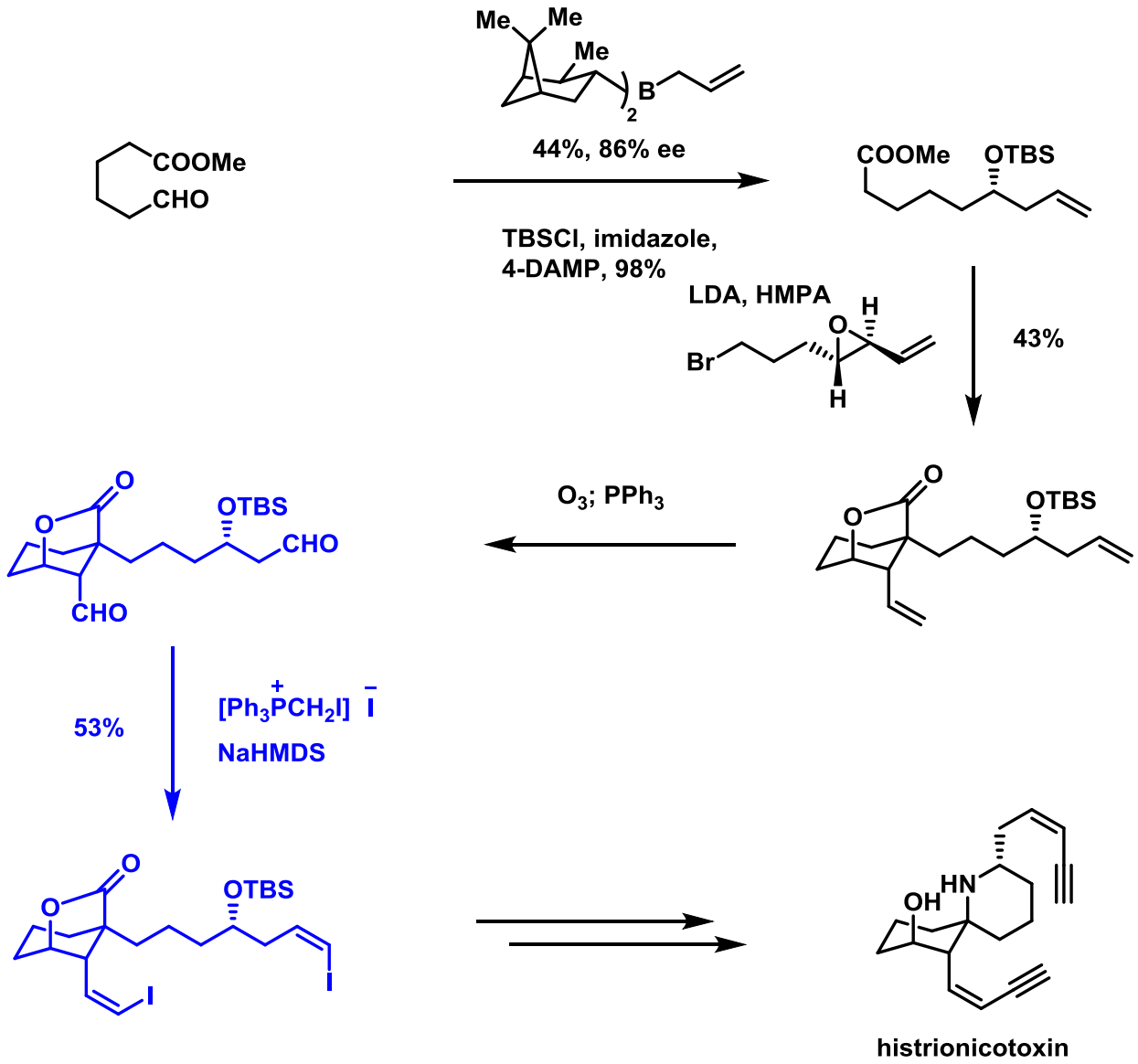


Besterman, et al. *Chem. Ber.* **1976**, *109*, 1694.



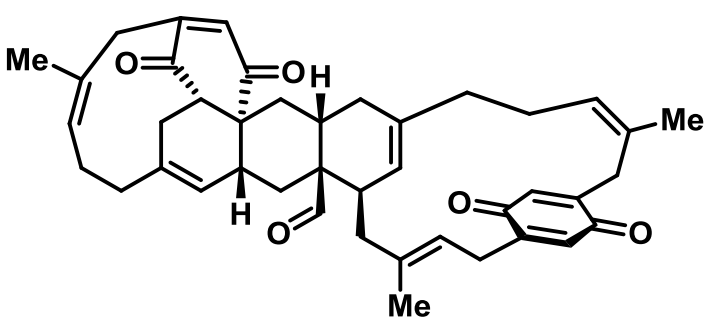
Nicolaou, et al. *J. Am. Chem. Soc.* **1995**, *117*, 1173.

卤代烯烃的合成：Stork–Zhao olefination

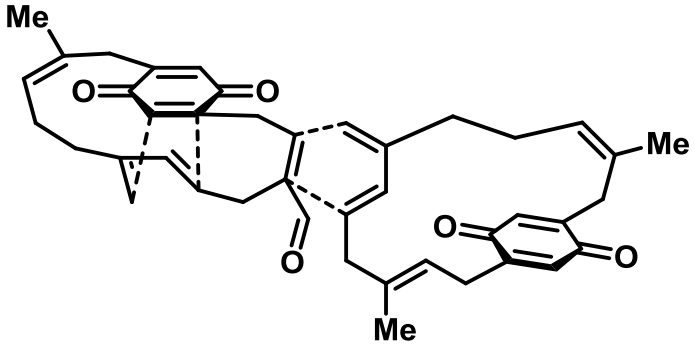


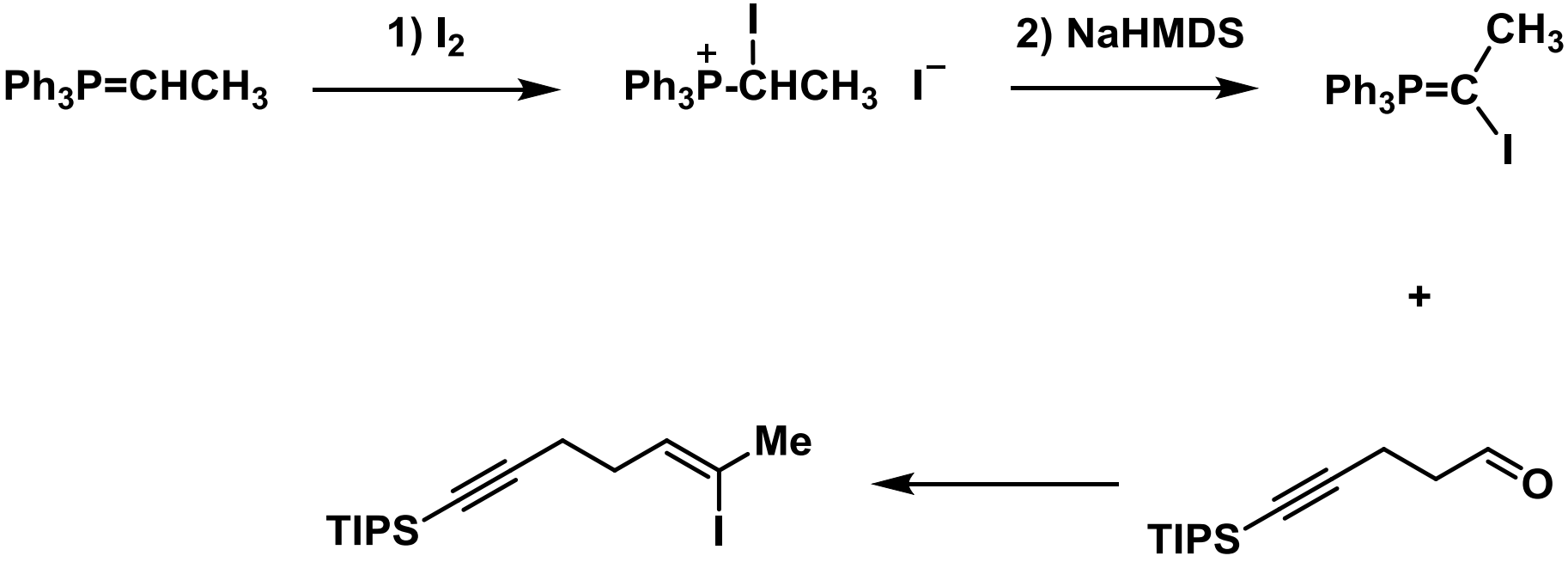
Stork, Zhao, *Tetrahedron Lett.* **1989**, *30*, 2173; *J. Am. Chem. Soc.* **1990**, *112*, 5876.

卤代烯烃的合成：Stork−Zhao olefination



longithorone A

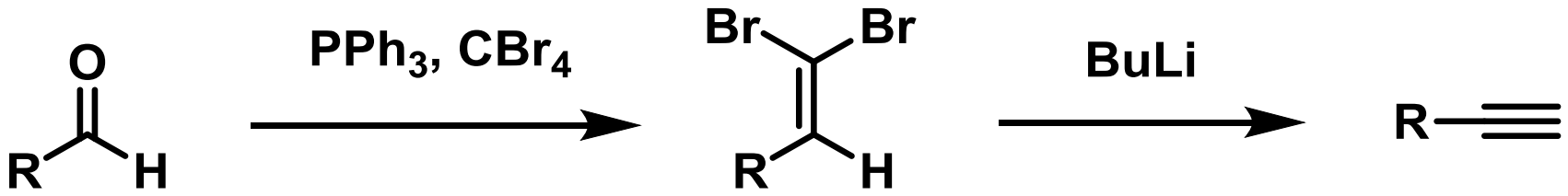




Shair, et al. *J. Am. Chem. Soc.* **2002**, *124*, 773.

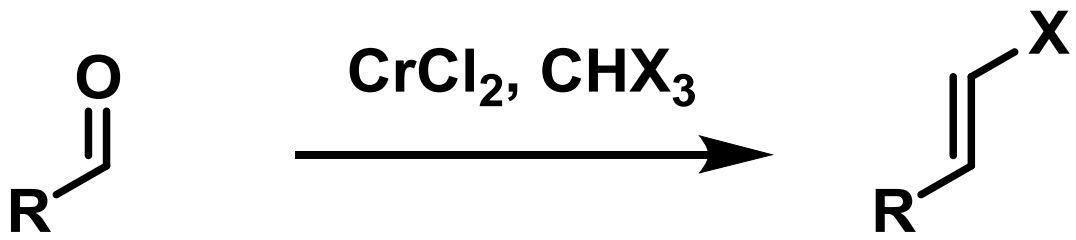
卤代烯烃的合成

Corey−Fuchs reaction



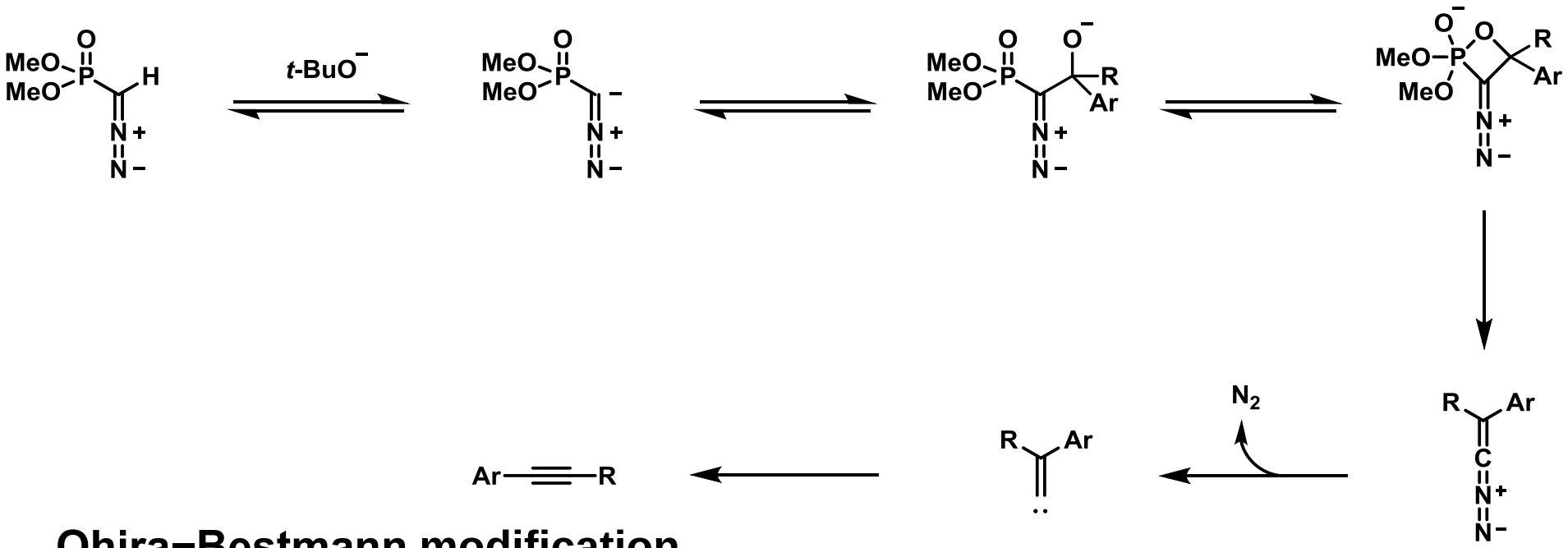
Corey, Fuchs, *Tetrahedron Lett.* **1972**, *13*, 3769.

Takai olefination

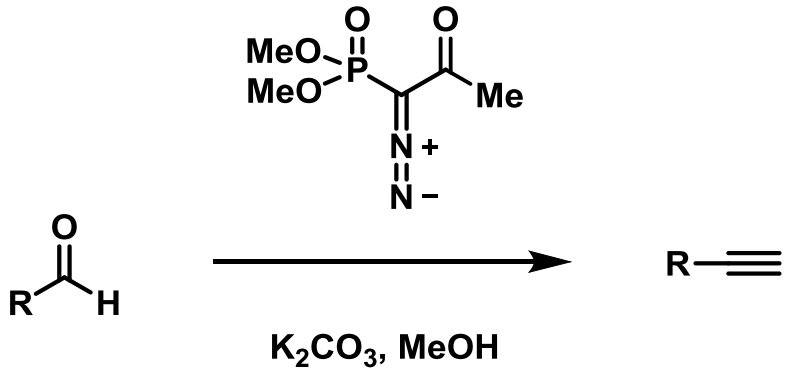


Takai, et al. *J. Am. Chem. Soc.* **1986**, *108*, 7408.

炔烃的合成：Seyferth–Gilbert homologation



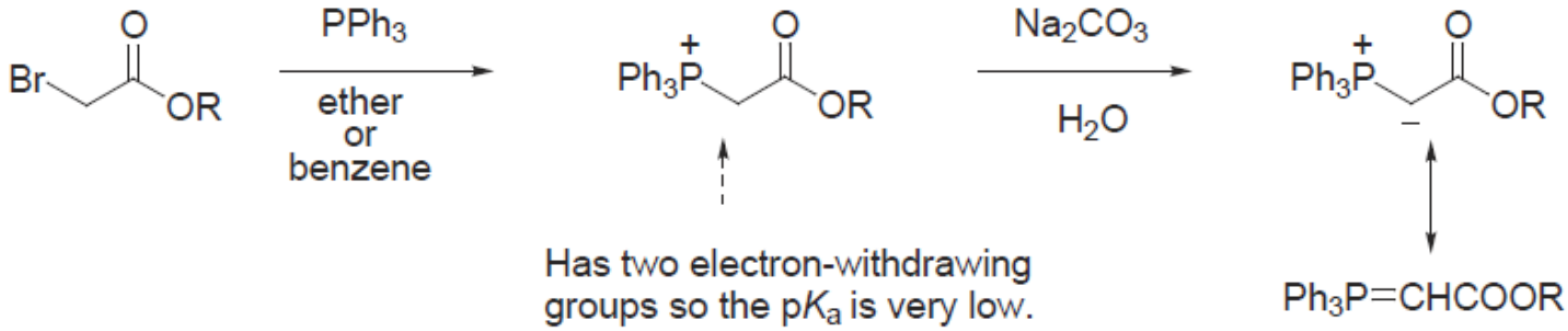
Ohira−Bestmann modification



Seyferth, et al. *J. Org. Chem*. **1971**, *36*, 1379; Gilbert and Weerasooriya, *J. Org. Chem.* **1982**, *47*, 1837.
Bestmann, et al. *Synlett* **1996**, 521.

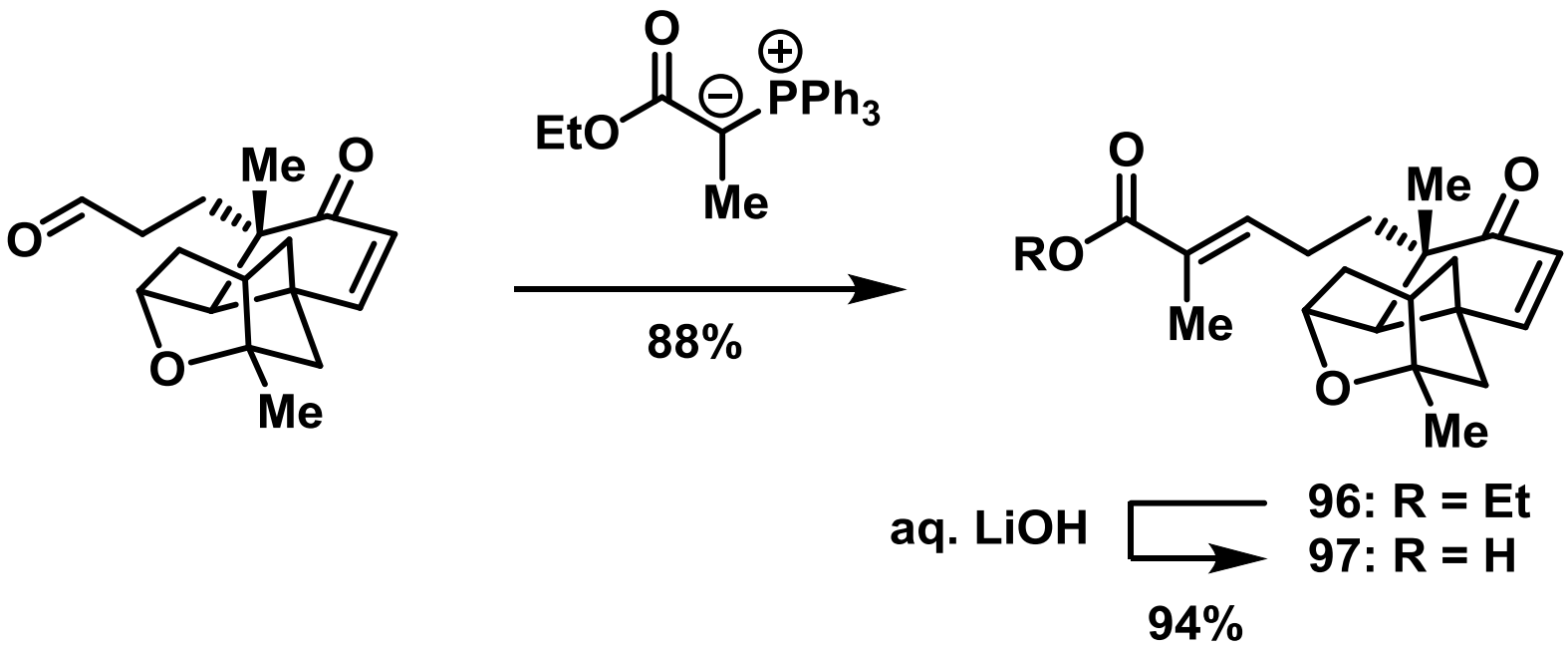
Wittig反应的中的稳定ylide

Stabilized Ylides



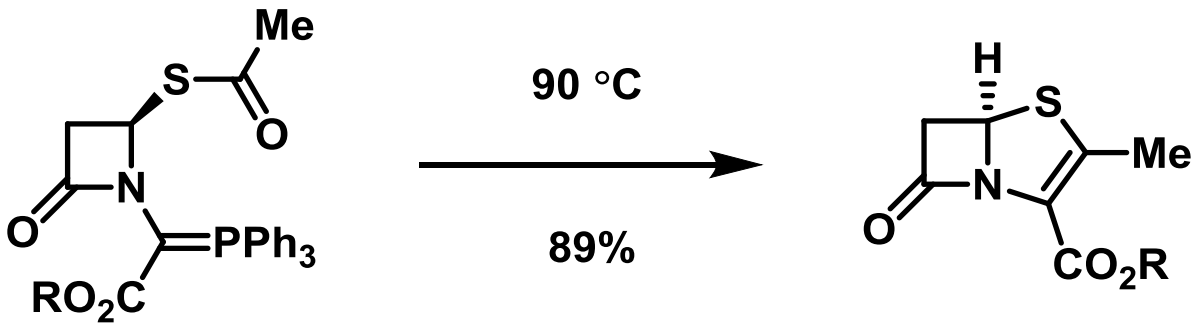
- Stabilized ylides are solid; stable to storage, not particularly sensitive to moisture, and can even be purified by chromatography.
- Because they are stabilized, they are much less reactive than alkyl ylides. They react well with aldehydes, but only slowly with ketones.
- The first step, involving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

Wittig反应的中的稳定ylide

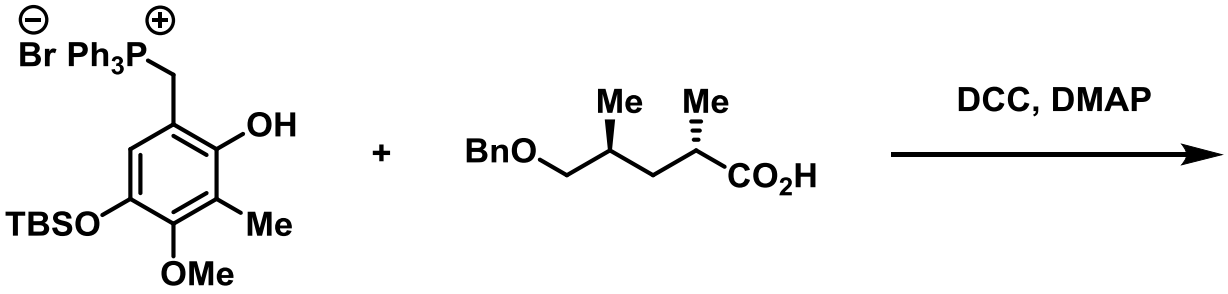


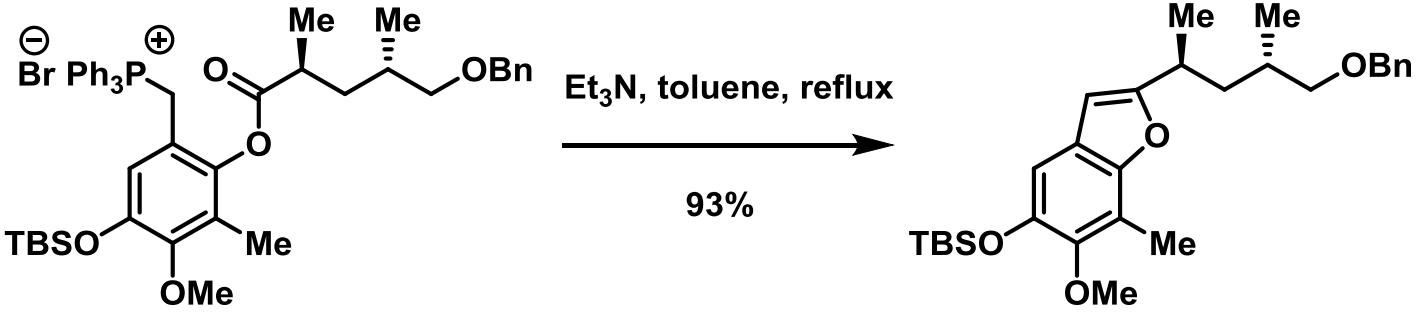
Nicolaou, et al. *J. Am. Chem. Soc.* **2009**, *131*, 16905.

Wittig反应的中的稳定ylide



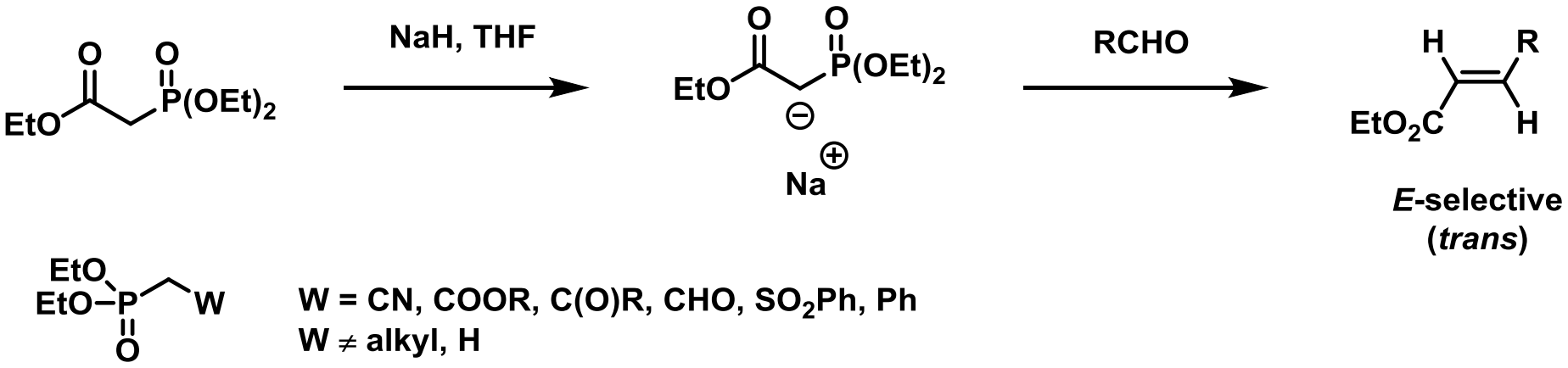
Woodward, et al. *J. Am. Chem. Soc.* **1979**, *101*, 6301.





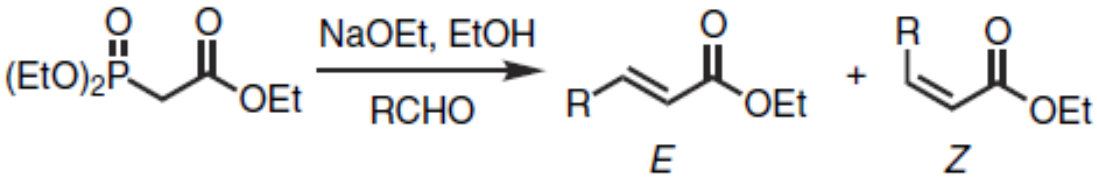
Lee, et al. *J. Am. Chem. Soc*. **2004**, *126*, 14720.

Horner–Wadsworth–Emmons反应



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

Horner–Wadsworth–Emmons反应



Aldehyde	Ratio of products (*E* : *Z*)
PhCHO	98 : 2
n-PrCHO	95 : 5
i-PrCHO	84 : 16

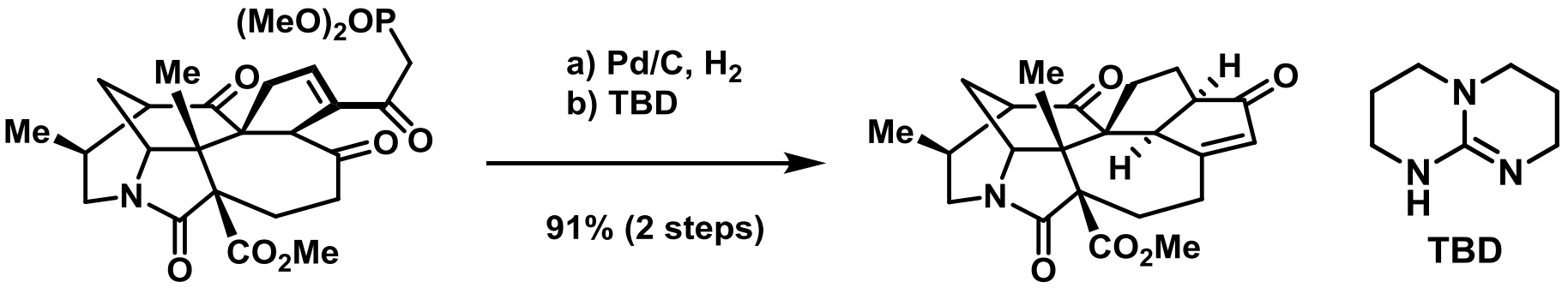
Larsen, R. O.; Aksnes, G. *Phosphorus Sulfur*, **1983**, *16*, 339-344.

• In a systematic study of the synthesis of disubstituted olefins by HWE, *E* : *Z* ratio increases:
(1) in DME relative to THF,
(2) at higher reaction temperatures,
(3) M^+ = Li > Na > K,
(4) with increasing α-substitution of the aldehyde.

In general, conditions which increase the reversibility of the reaction (i.e., increase the rate of retroaddition relative to the rate of elimination) favor the formation of *E*-alkenes.

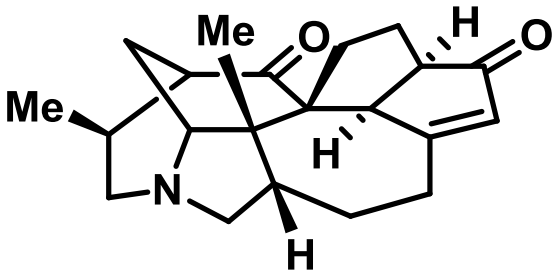
Thompson, S. K.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 3386-3388.

Horner–Wadsworth–Emmons反应



Li, et al. *J. Am. Chem. Soc.* **2017**, *139*, 14893.

问题：
为什么是这样的反应次序？



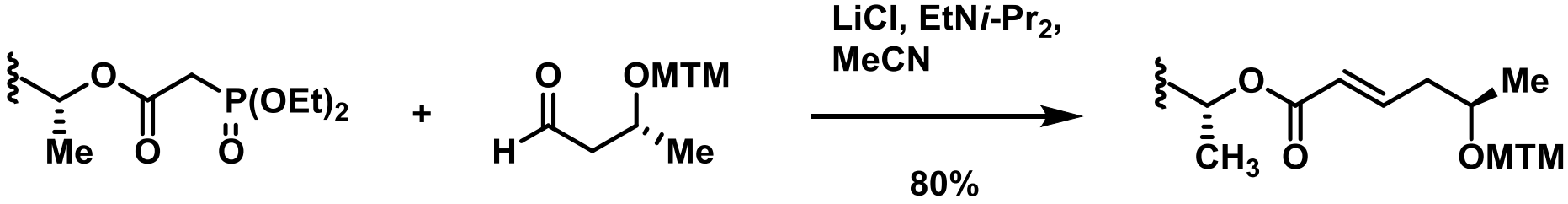
daphniyunnine C
(longeracinphyllin A)

Horner–Wadsworth–Emmons反应

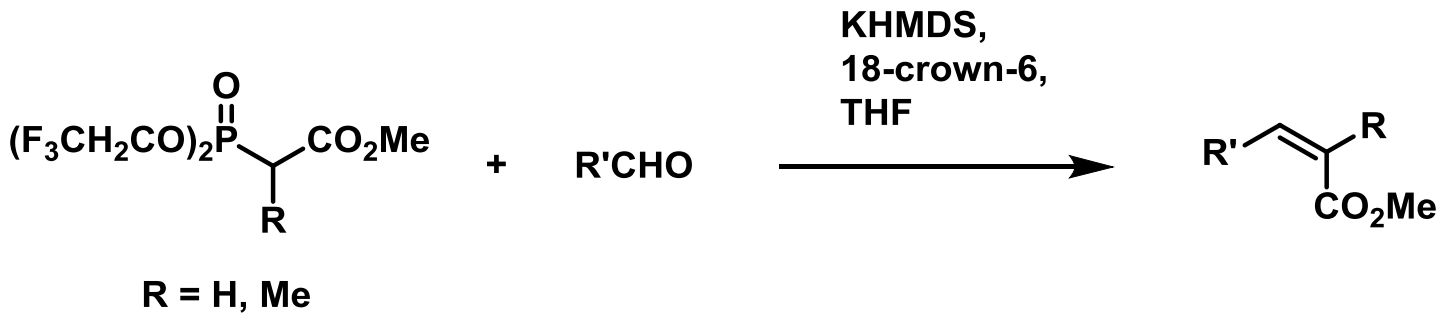
Masamune–Roush conditions

- 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).



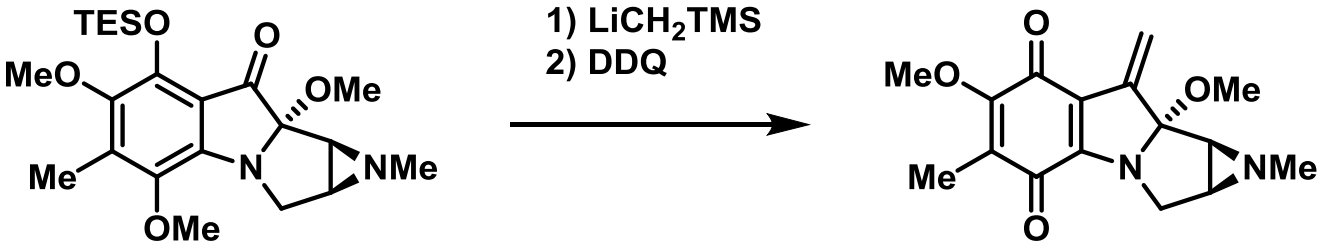
Still–Gennari modification



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

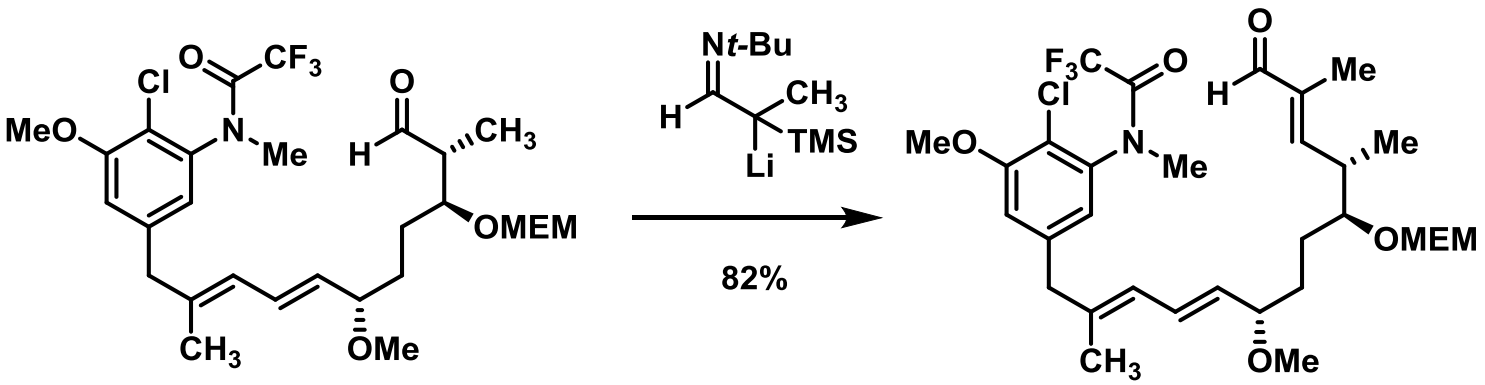
Peterson反应

Nonstabilized Peterson Reagents



Danishefsky, et al. *J. Org. Chem.* **1988**, *53*, 3391.

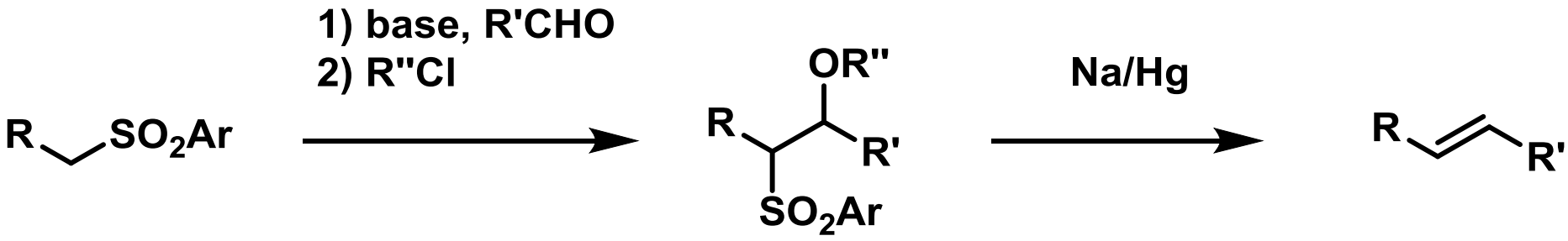
Stabilized Peterson Reagents



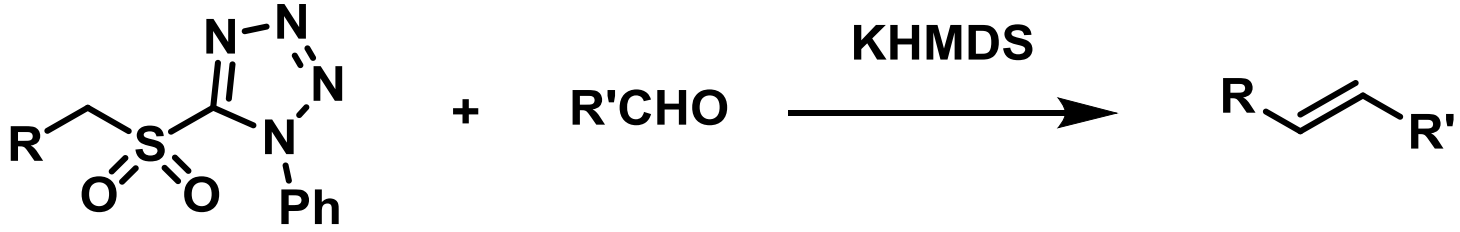
Corey, et al. *J. Am. Chem. Soc.* **1980**, *102*, 1439.

问题：
还有什么试剂可以实现这种转化？

Julia反应

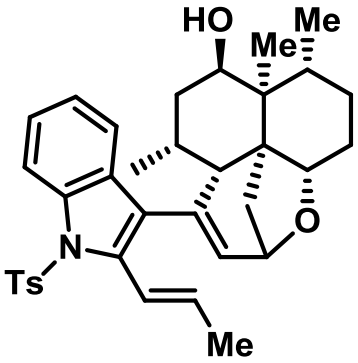


R'' = Ms, Ts, Ac, COPh



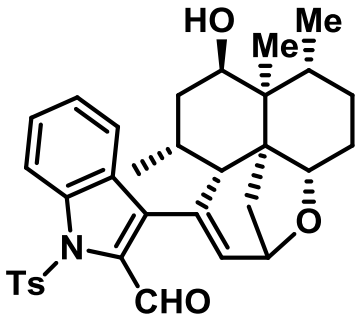
Kocieński, et al. *Synlett* **1998**, 26.

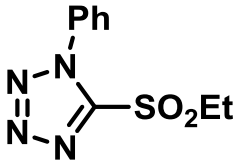
Julia–Kocieński反应



LiHMDS, 2

86%

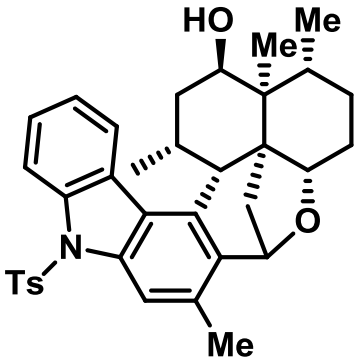




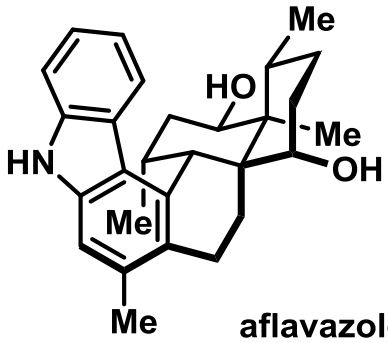
2

82%

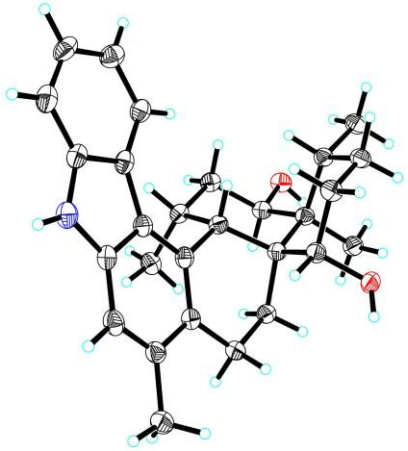
toluene, 90 °C;
then DDQ



1) $TiCl_4$, Et_3SiH, 80%
2) Mg, MeOH, 96%

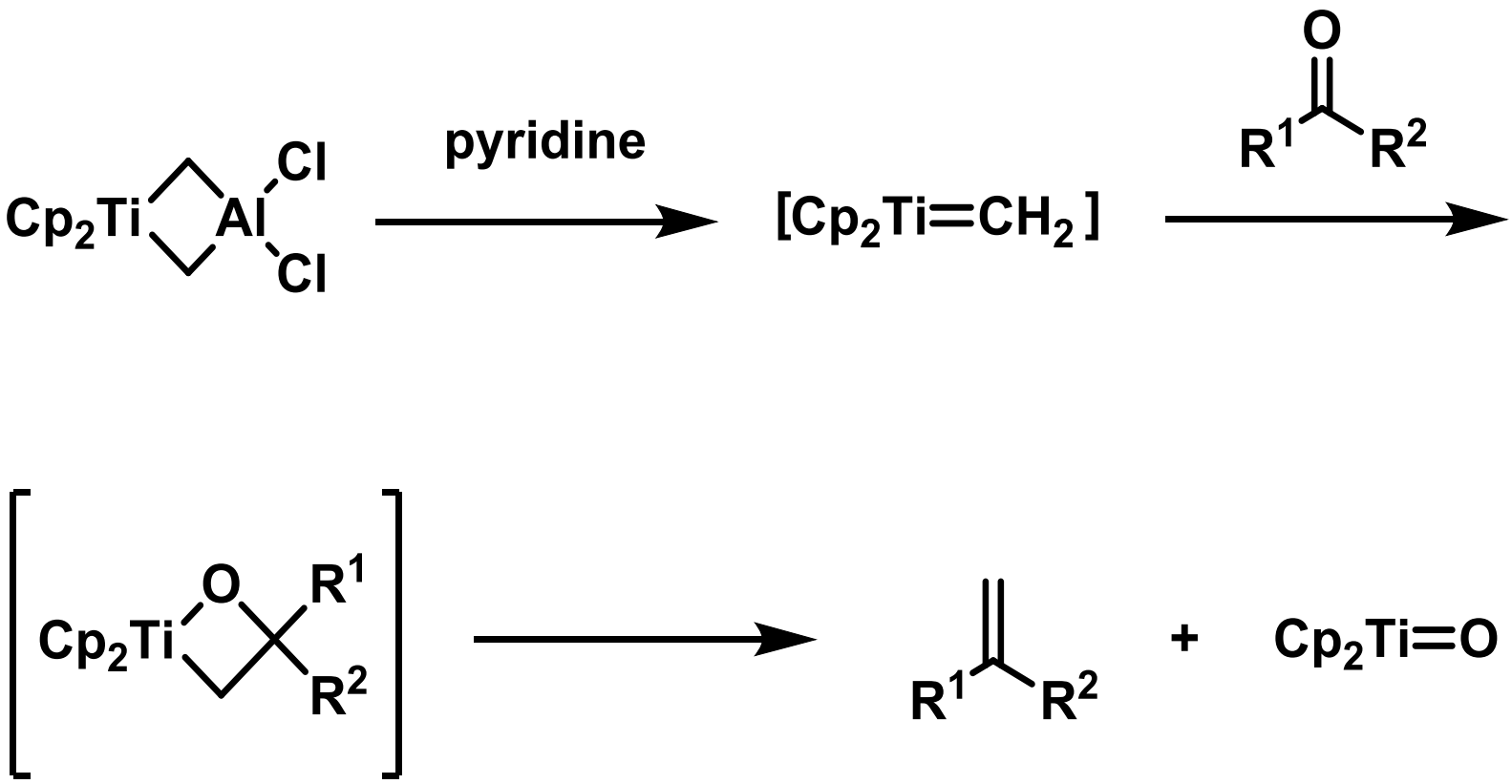


aflavazole



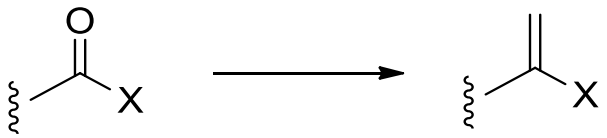
Li, et al. *J. Am. Chem. Soc.* **2016**, *138*, 15555.

Tebbe反应

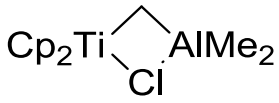


Hughes, et. al. *Organometallics.* **1996**, *63*, 2689.

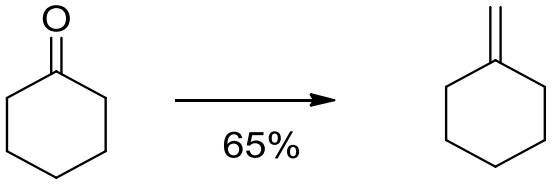
Tebbe反应

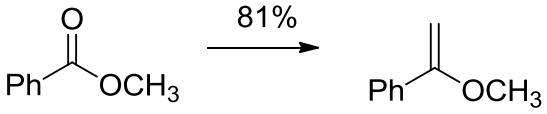


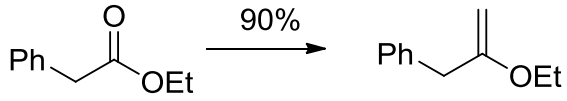
X= H, R, OR, NR_2

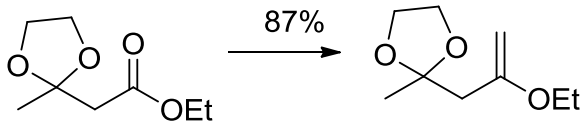


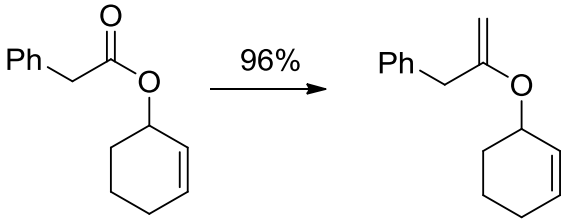
Tebbe reagent

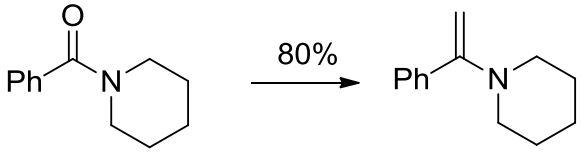












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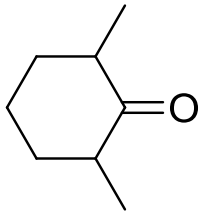
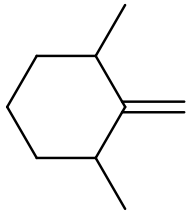
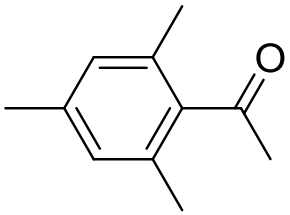
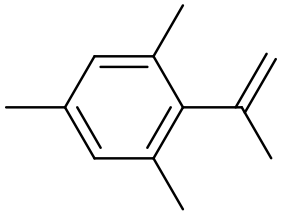
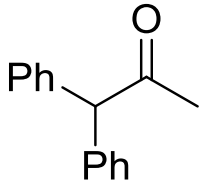
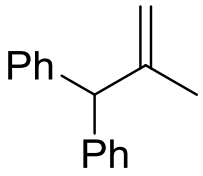






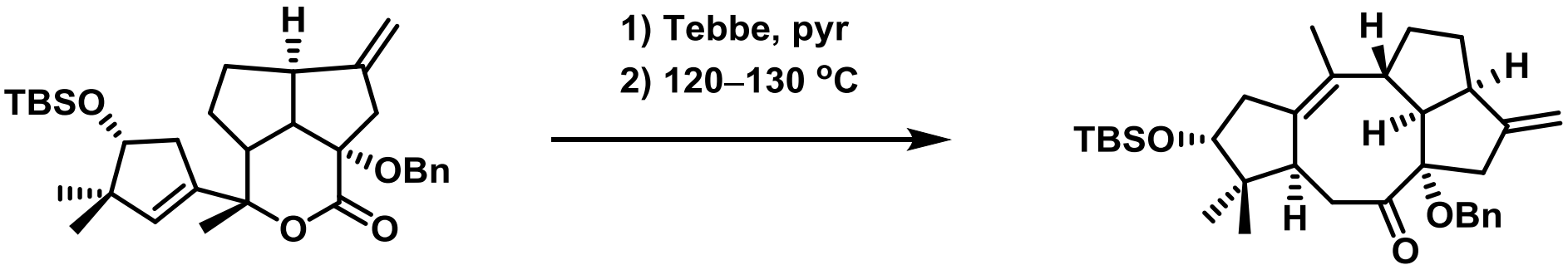






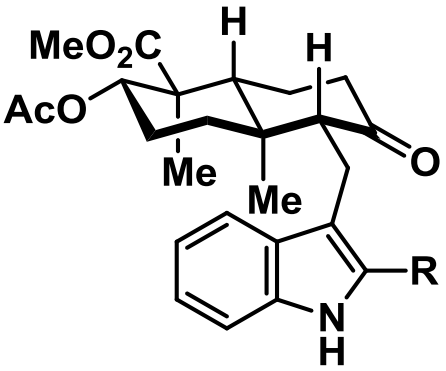
	Tebbe	Witting
	97%	89%
	77%	4%
	63%	38%

Tebbe反应



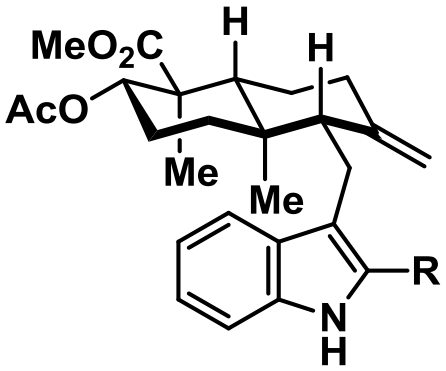
Paquette, et al. *J. Am. Chem. Soc*. **1996**, *118*, 727.

Nysted试剂

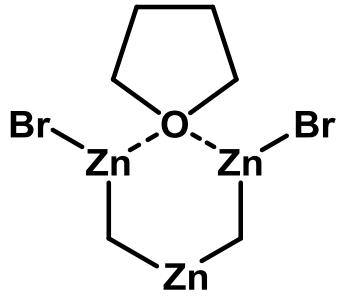


1: R = H
2: R = CO_2Me

$TiCl_4$, Nysted reagent



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



Nysted reagent

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谢　谢！

2018年11月26日