五、一些形成C–C键的基本反应
（三）自由基参与的反应

李昂

中国科学院上海有机化学研究所
生命有机化学国家重点实验室

2018年11月12日

一、概论
二、基础知识
构象分析
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
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
自由基反应
烯基化反应
六、周环反应
非直观Diels-Alder反应
1,3-偶极环加成反应
电环化反应
sigmatropic重排
七、阳离子参与的C–C键形成反应

自由基参与的C-C键形成反应：基本过程

引发

$$In\bullet + R'_3SnH \rightarrow R'_3Sn\bullet + In{-}H$$

增长

$$R{-}X + R'_3Sn\bullet \rightarrow R\bullet + R'_3Sn{-}X$$

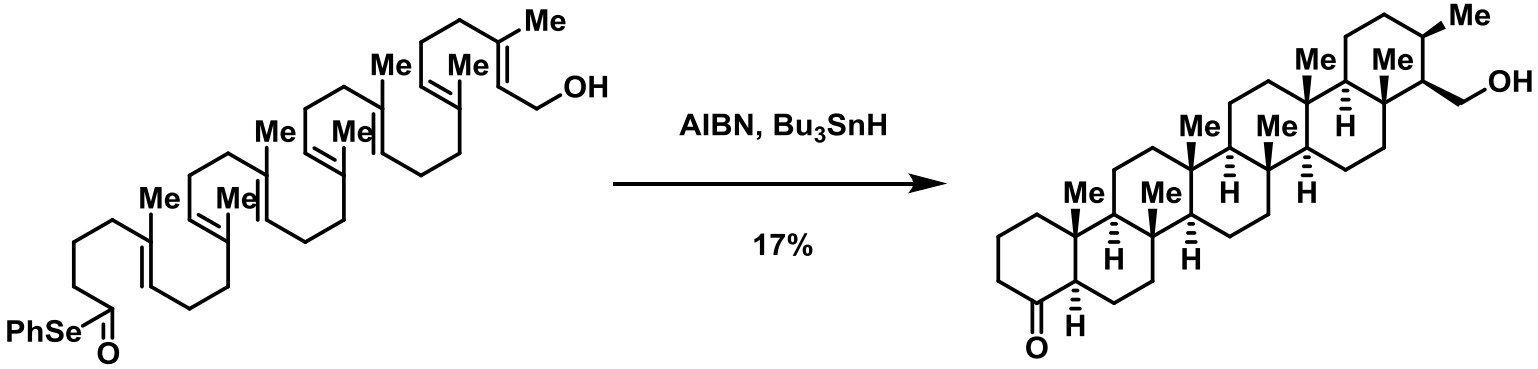
$$R\bullet + Y{=}Z \rightarrow R{-}Y{-}Z\bullet$$

$$R{-}Y{-}Z\bullet + R'_3SnH \rightarrow R{-}Y{-}Z{-}H + R'_3Sn\bullet$$

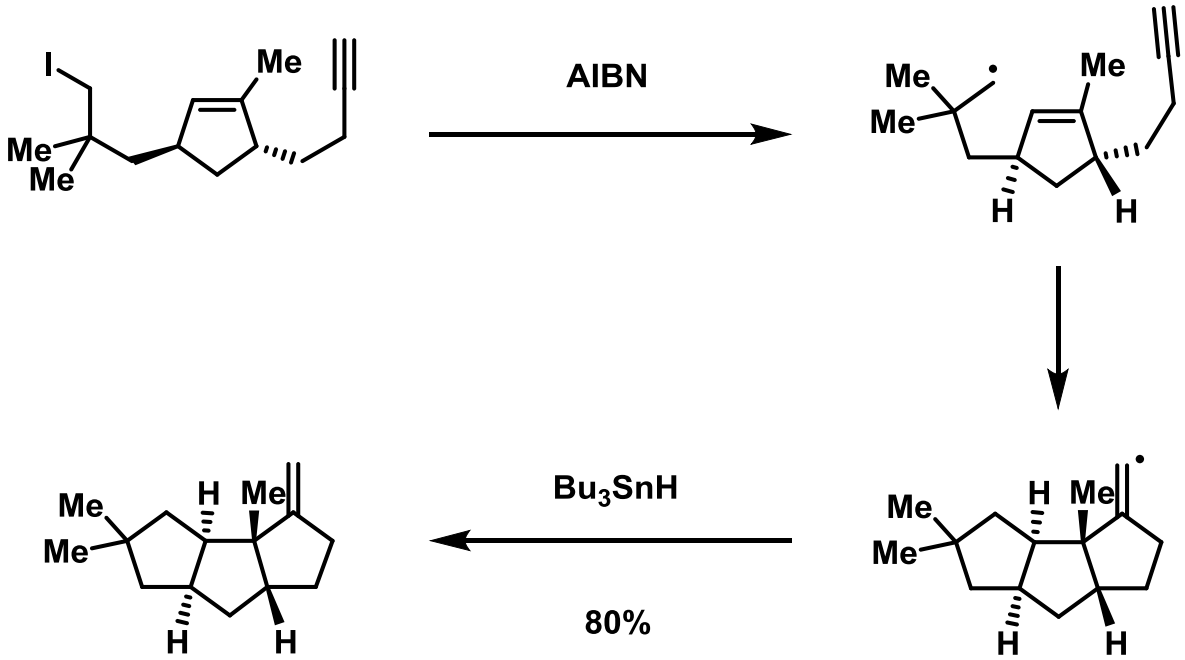
自由基参与的C–C键形成反应：优点

- Neutral reaction conditions
- Compatibility with radical acceptors containing functional groups – carbonyls, enol ethers, and enamines
- Compatibility with Lewis acids
- No necessity for protection of alcohol and amine functional groups
- Compatibility with protic solvents – potential for reaction in aqueous systems
- Ease of quaternary center formation

自由基的优点：两个经典实例

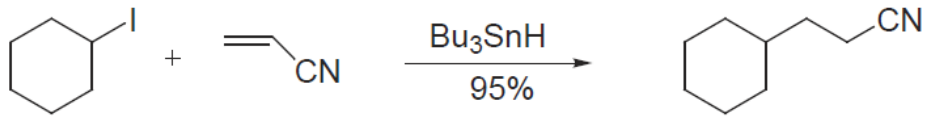


G. Pattenden, et al. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 843.



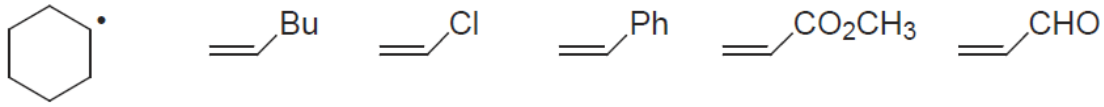
D. P. Curran, et al. *J. Am. Chem. Soc.* **1985**, *107*, 1448.

自由基参与的C–C键形成反应：电子效应

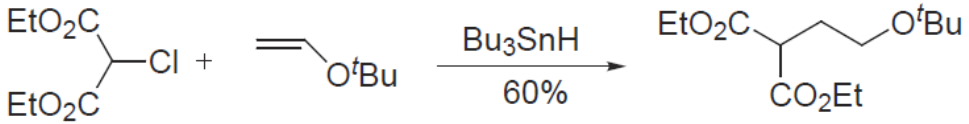


Nucleophilic radical

Electrophilic acceptor alkene

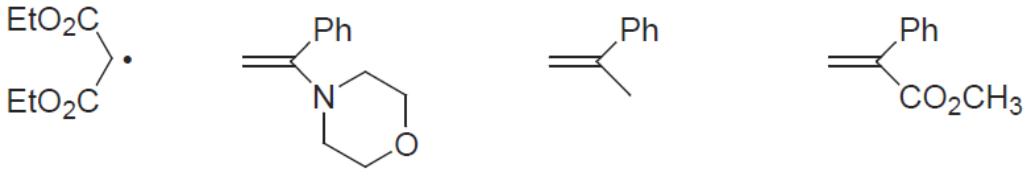


k_{rel}	1.0	8.4	84	3000	8500



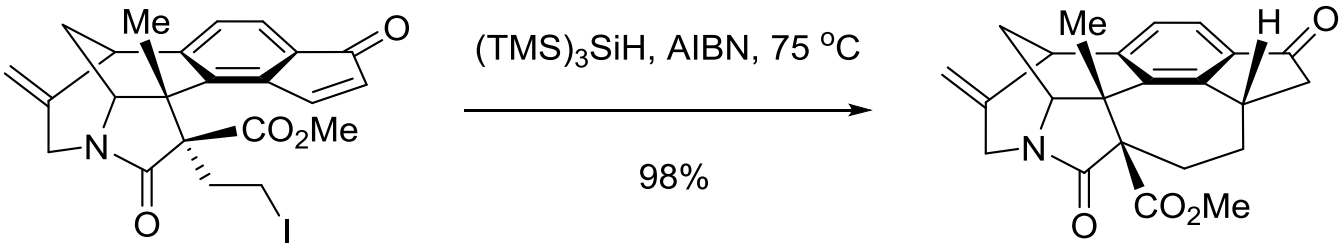
Electrophilic radical

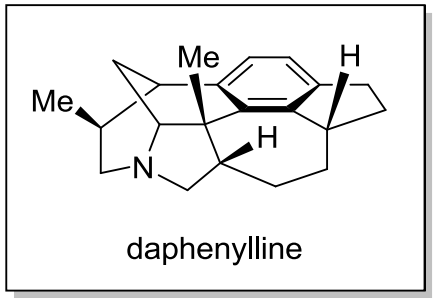
Nucleophilic acceptor alkene



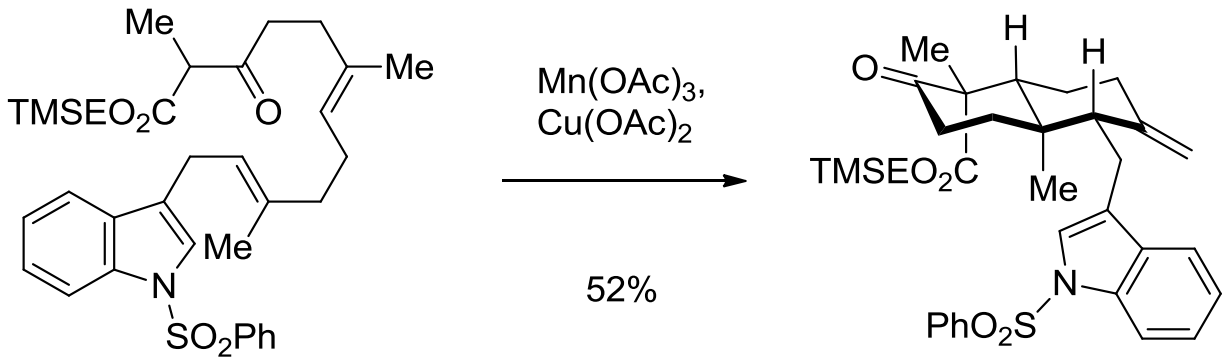
k_{rel}	23	3.5	1

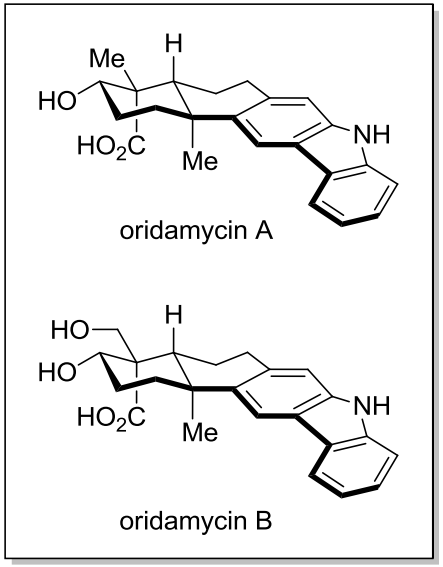
自由基参与的C–C键形成反应：电子效应的两个实例





Z. Lu, Y. Li, J. Deng, A. Li, *Nature Chem.* **2013**, *5*, 679.

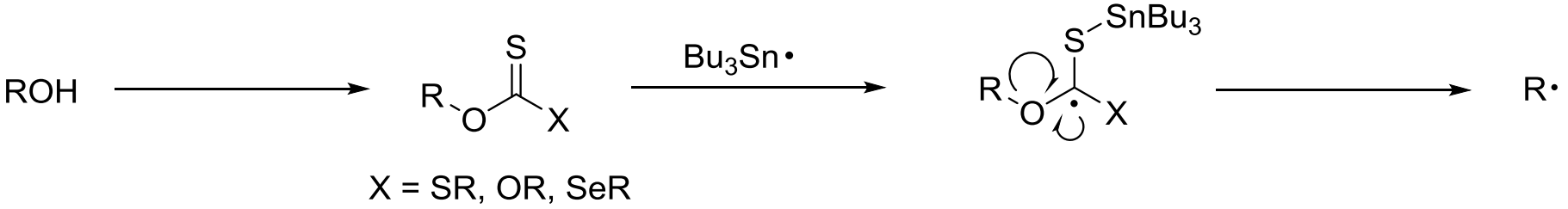




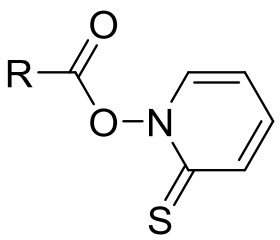
Z. Meng, H. Yu, … A. Li, *Nature Commun.* **2015**, *6*, 6096.

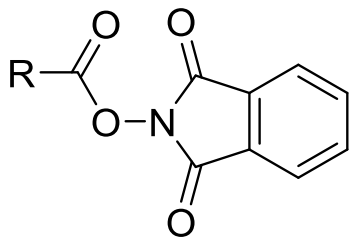
自由基参与的C–C键形成反应：引发官能团

Initiator Groups

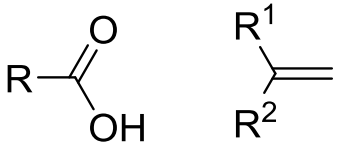


X = SR, OR, SeR





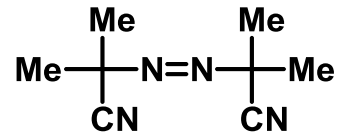
R–H (C–H oxidation)



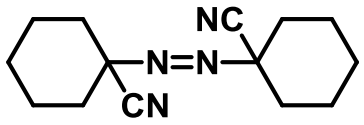
自由基参与的C–C键形成反应：引发剂、氢化物

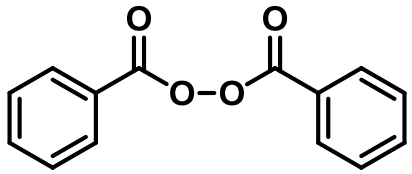
引发剂

AIBN:



ACCN (V-40):





Et_3B/O_2, Et_2Zn/O_2, Me_3Al/O_2

UV light

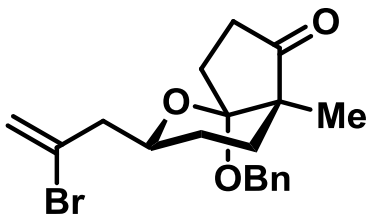
Ru/Ir complex or organic dye, visible light (photoredox)

Metal hydride

氢化物

Bu_3SnH, $(TMS)_3SiH$

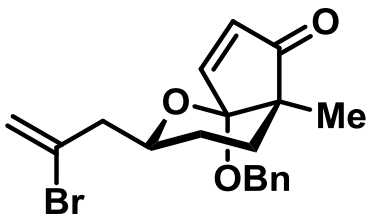
官能化的自由基



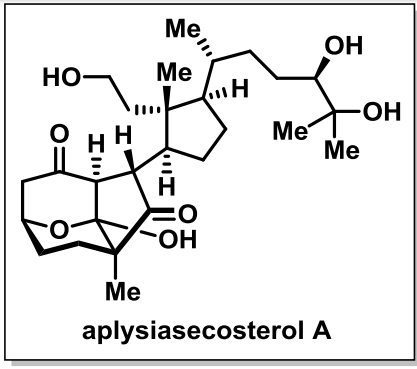
22

i) TMSOTf, Et_3N
j) IBX, MPO

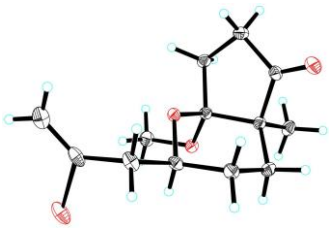
82% (2 steps)



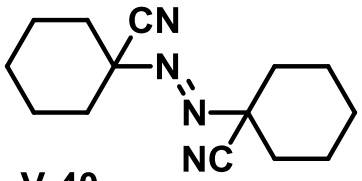
11



aplysiasecosterol A



ORTEP of the methoxy analogue of **22**

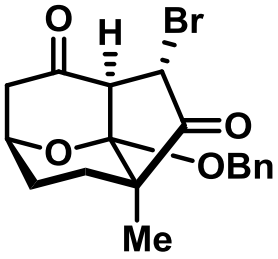


V-40

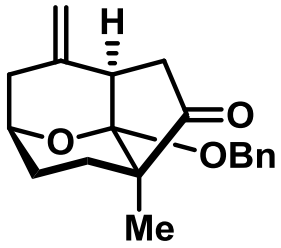
k) $(TMS)_3SiH$, V-40, 110 °C, 78%
or Bu_3SnH, AIBN, 100 °C, 23%

l) KHMDS, TMSCl
m) NBS
n) O_3; Me_2S

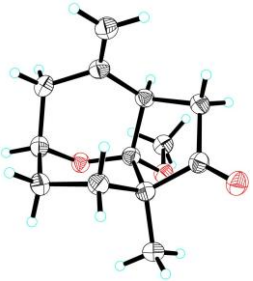
91% (3 steps)



9



23

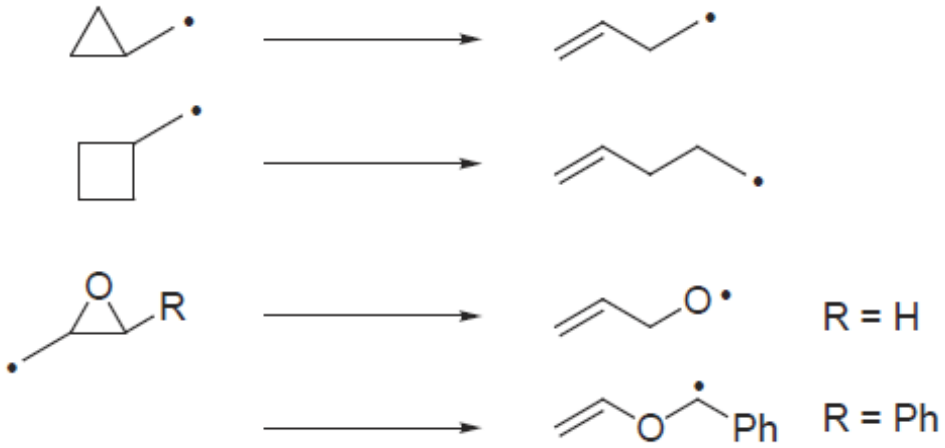


ORTEP of the methoxy analogue of **23**

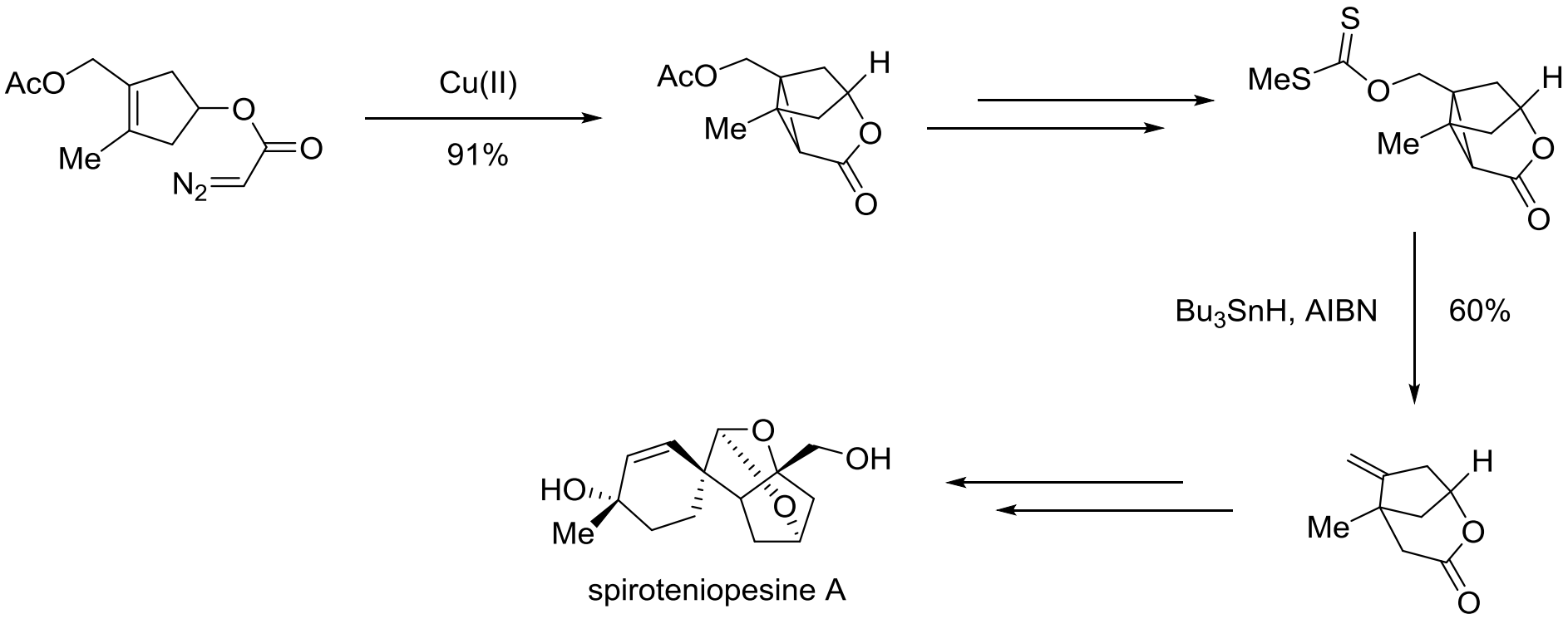
Z. Lu, X. Zhang, Z. Guo, Y. Chen, T, Mu, A. Li, *J. Am. Chem. Soc.* **2018**, *140*, 9211.

自由基引发的断裂反应

Radical clock: 可用于检验反应中是否涉及自由基中间体

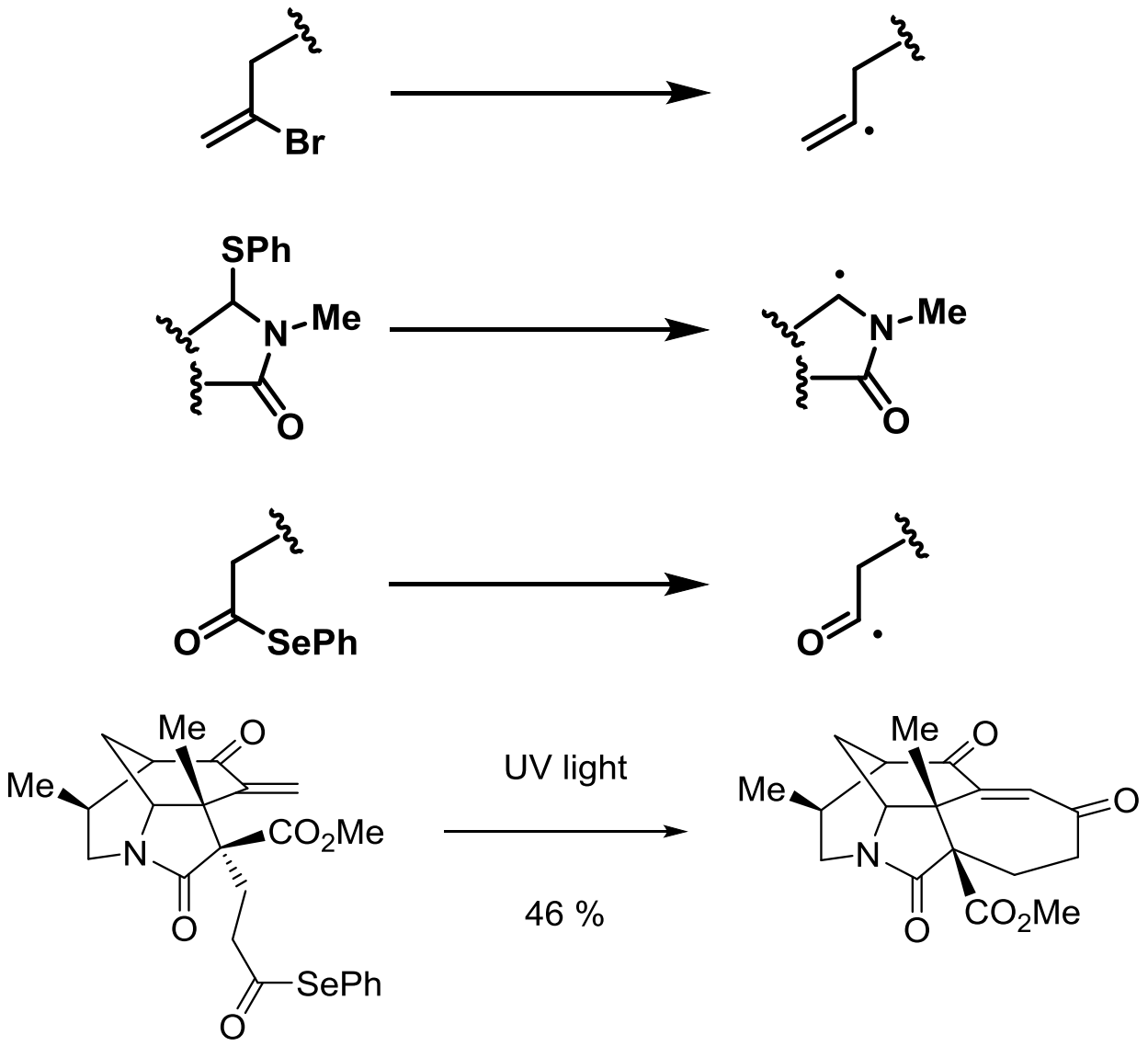


自由基引发的断裂反应的应用



M. Dai, S. J. Danishefsky, *J. Am. Chem. Soc.* **2007**, *129*, 3498.

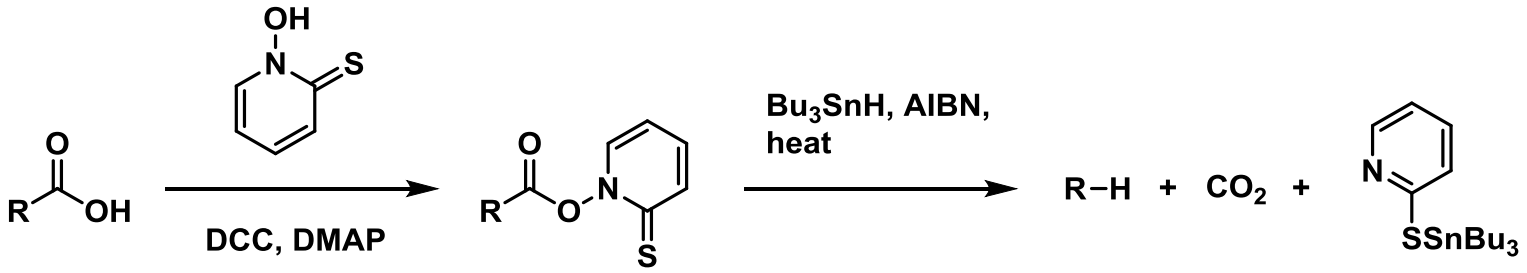
官能化的自由基



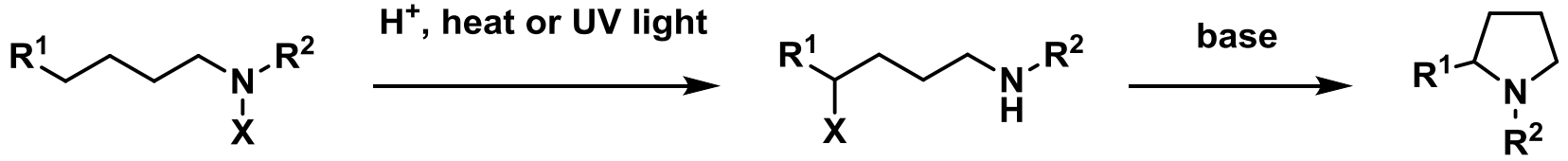
Y. Chen, W. Zhang, L. Ren, J. Li, A. Li, *Angew. Chem. Int. Ed.* **2018**, *57*, 952.

几个重要的自由基人名反应

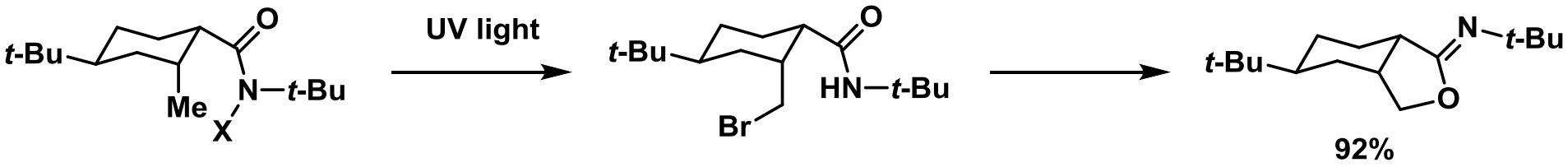
Barton decarboxylation



Hofmann–Löffler–Freytag reaction



X = Cl, Br, I



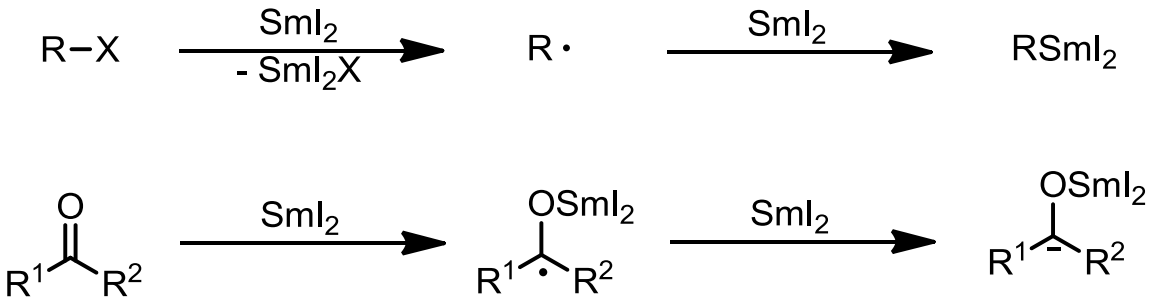
92%

Y. L. Chow, T. W. Mojelsky, L. J. Magdzinski, M. Tichy, *Can. J. Chem.* **1985**, *63*, 2197.

SmI_2的基本性质

制备：Sm/I_2, Sm/ICH_2CH_2I
性质：reduction potential up to 2.05 V in the presence of HMPA
Aldrich：0.1 M/100 mL, 625.95 RMB

a) SmI_2-mediated activation of alkyl hlides

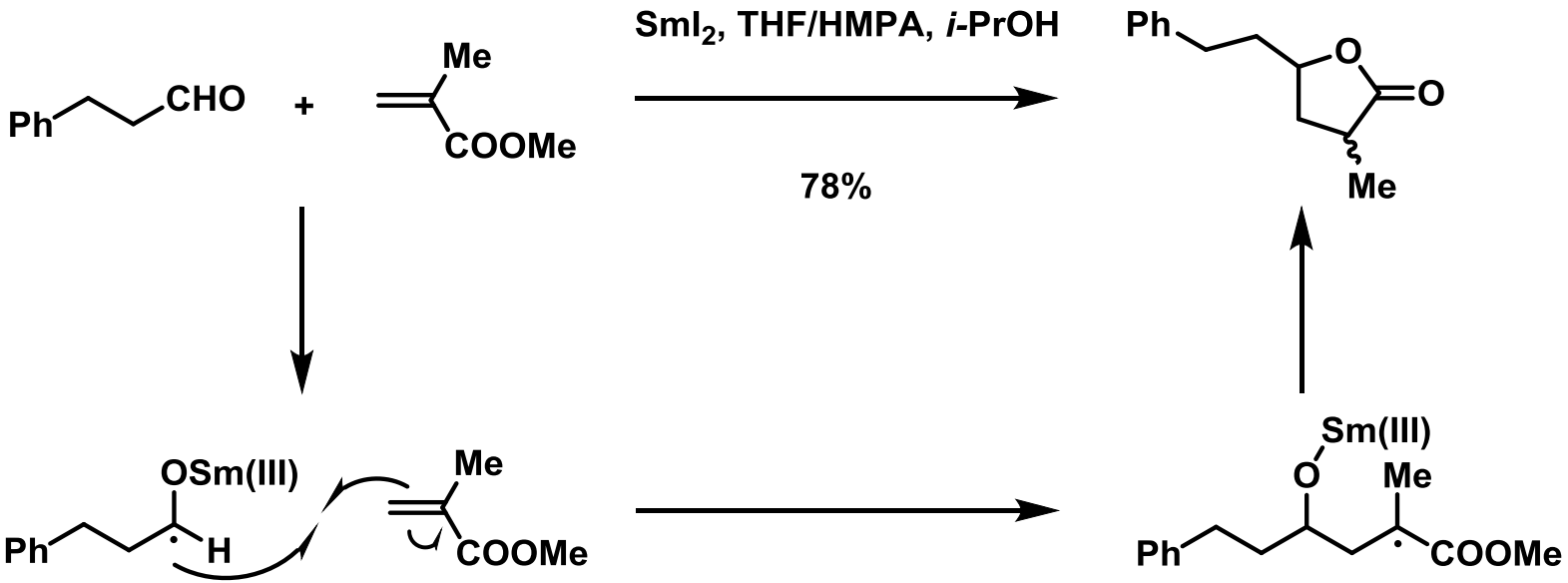


- Barbier reaction
- Ketyl-olefin coupling reaction
- Pinacol type coupling reaction
- Reduction

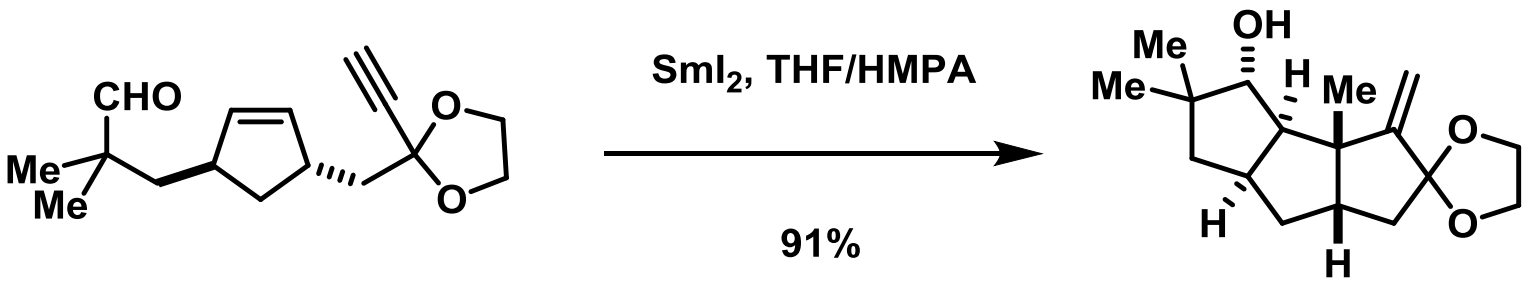
P. Girard, J. L. Namy and H. B. Kagan “Divalent Lanthanide Derivatives in Organic Synthesis. 1. Mild Preparation of SmI_2 and YbI_2 and Their Use as Reducing or Coupling Agents”. *J. Am. Chem. Soc.* **1980**, *102* , 8, 2693.

K. C. Nicolaou, S. P. Ellery, J. S. Chen. “Samarium Diiodide Mediated Reactions in Total Synthesis”. *Angew. Chem. Int. Ed.* 2009, **48**, 7140.

SmI_2参与的C–C键形成反应：羰基-烯烃偶联



Inanaga, *Tetrahedron Lett.* **1986**, *27*, 5763.



Curran, *J. Am. Chem. Soc.* **1988**, *110*, 5064.

谢　谢！

2018年11月12日