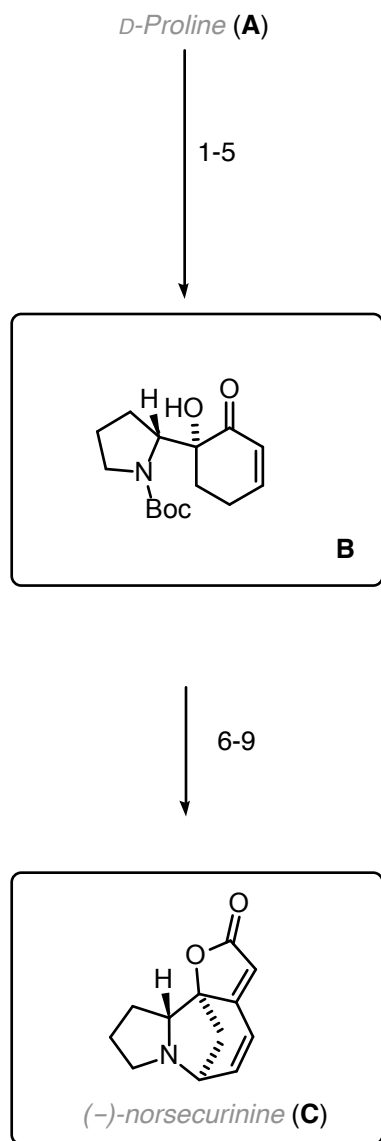


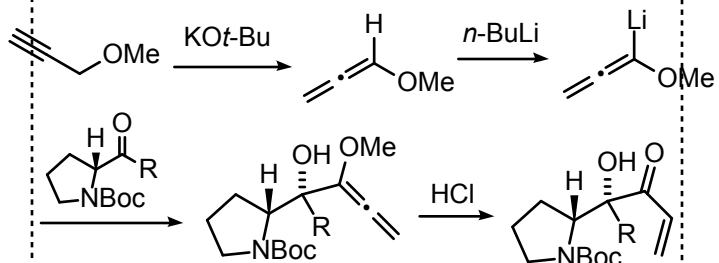
# Total synthesis of securinega alkaloids (-)-norsecurinine, (-)-niruroidine and (-)-flueggine A

Nan Ma, Yiwu Yao, Bing-Xin Zhao, Ying Wang, Wen-Cai Ye and Sheng Jiang, *Chem. Commun.* **2014**, 50, 9284–9287.



- 1) (Boc)<sub>2</sub>O, NaHCO<sub>3</sub>
- 2) CDI, MeNHOMe·HCl, DCM
- 3) 4-Bromo-1-butene, BrCH<sub>2</sub>CH<sub>2</sub>Br, Mg
- 4) Methyl propargyl ether, KO<sup>t</sup>Bu; *n*-BuLi  
then product of Step 3; HCl
- 5) 2<sup>nd</sup> generation Grubbs catalyst

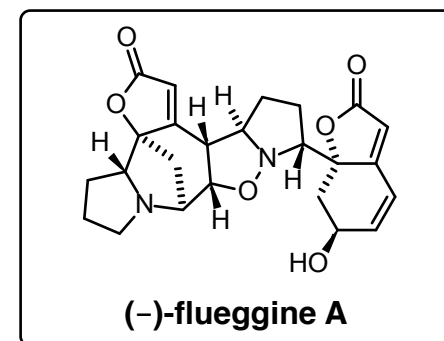
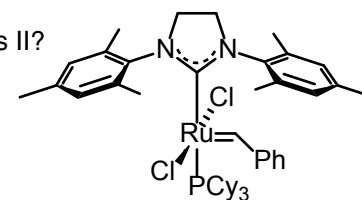
Mechanism of Step 4



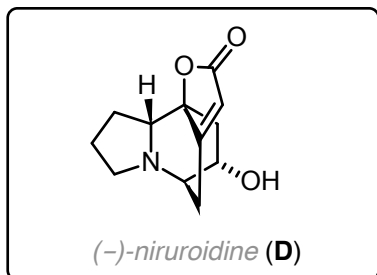
- 6) NBS, AIBN, CCl<sub>4</sub>, reflux
- 7) TFA, then Et<sub>3</sub>N
- 8) DCC, diethylphosphonoacetic acid
- 9) NaH, THF

Step 3: What is the role of BrCH<sub>2</sub>CH<sub>2</sub>Br?  
*Activation of the magnesium surface*  
Mechanism of Step 4.

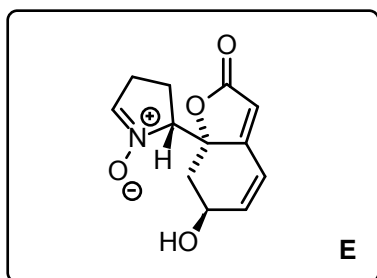
Structure of Grubbs II?



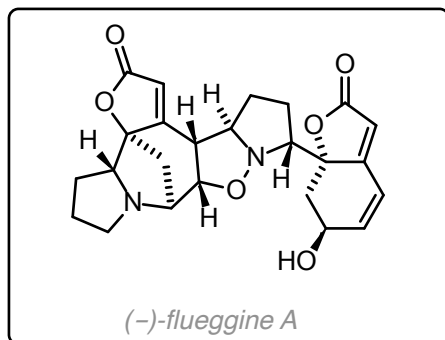
10-12



13-15



16



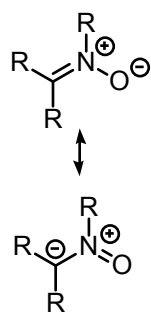
- 10) TrocCl, K<sub>2</sub>CO<sub>3</sub>
- 11) AgBF<sub>4</sub>, acetone, H<sub>2</sub>O, 60 °C
- 12) Zn, AcOH, H<sub>2</sub>O  
then NH<sub>3</sub>·H<sub>2</sub>O

Further methods for nitrene formation:

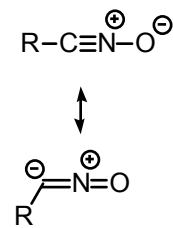
- 13) Dess-Martin periodinane
- 14) NaBH<sub>4</sub>, MeOH
- 15) Na<sub>2</sub>WO<sub>4</sub>, H<sub>2</sub>O<sub>2</sub>

- 16) *(-)-norsecurinine (C)*, PhMe, reflux

**Allyl anion type**



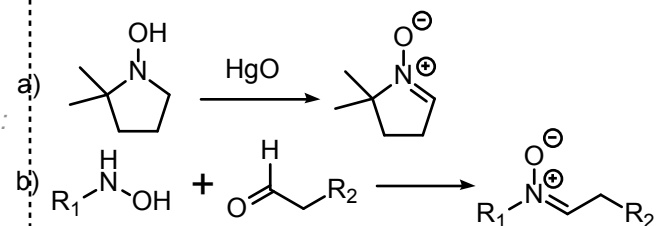
**Propargyl/allenyl anion type**



Step 11 results in a single diastereomer. Explain this exclusive selectivity.

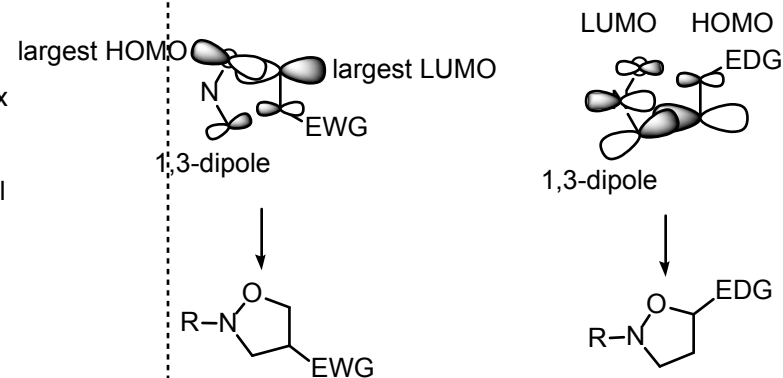
*neighboring group participation (anchimeric assistance)*

Treatment of **D** with PPh<sub>3</sub> and DIAD results in an efficient skeletal rearrangement (87%). Please provide the product and a possible mechanism for this transformation.



Please provide a mechanism for Step 15.  
What other methods for forming this 1,3-dipole do you know?

Assign the 1,3-dipole to its respective type.  
Explain the regiochemistry of this reaction by frontier orbital interactions.

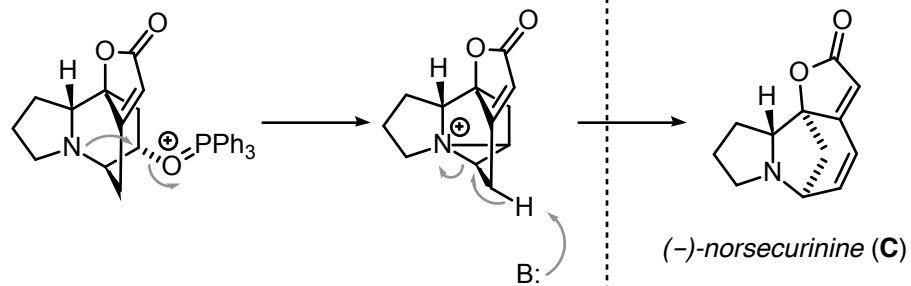


*EWG = electron withdrawing group*

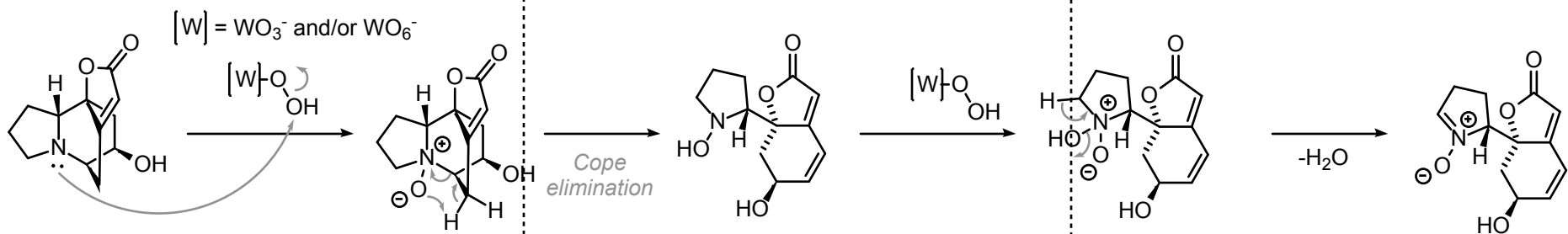
*EDG = electron donating group*

*The overlap of the highest orbital coefficients of HOMO and LUMO determine the regioselectivity*

Treatment of **D** with  $PPh_3$  and DIAD



Mechanism of Step 13<sup>[4]</sup>



4) S. Murahashi, H. Mitsui, T. Shiota, T. Tsuda and S. Watanabe, *J. Org. Chem.* **1990**, 55, 1736.

#### References

- 1) Brueckner, R. "Organic Mechanisms — Reactions, Stereochemistry and Synthesis", pages 674–686.
- 2) Sustmann, R. *Heterocycles* **1995**, 40, 1-18.
- 3) Houk, K. N. *JACS* **1972**, 94, 8953.