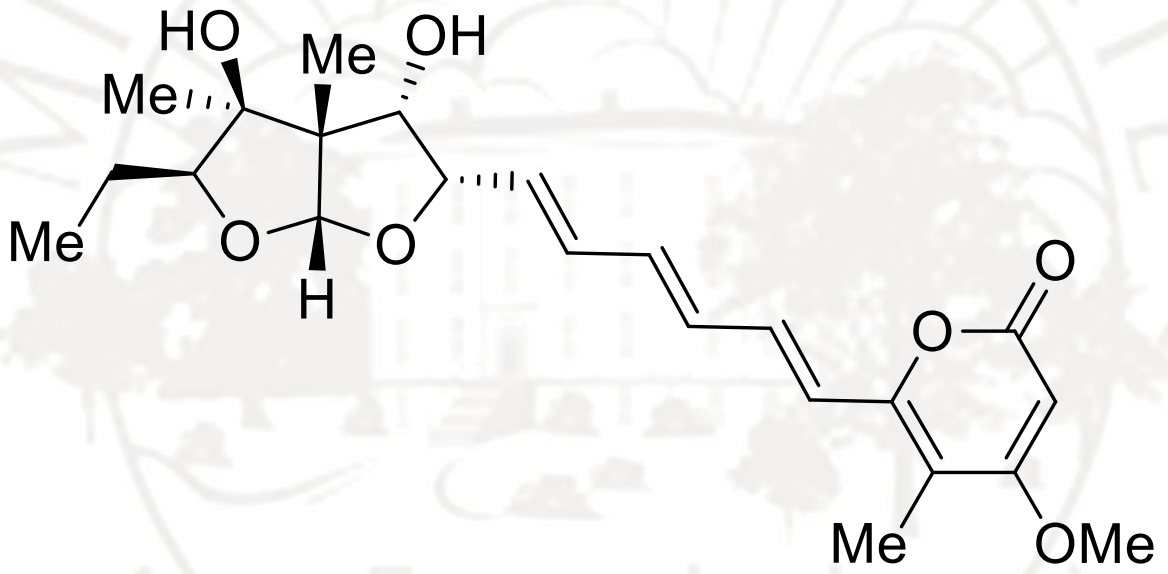
ASTELTOXIN

By:

Milad Pedarpour Vajargahy

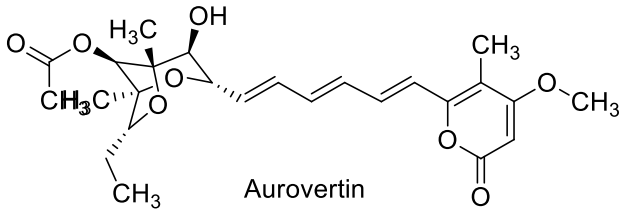
Teacher: Prof. Maleczka

CEM852

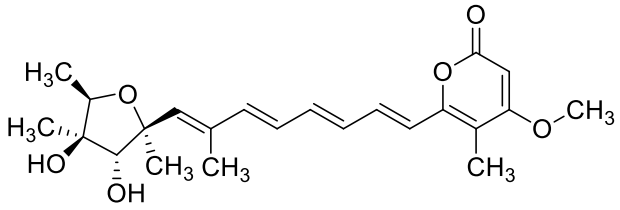


Introduction

- The toxic maize cultures of Aspergillus stellatus contain a mycotoxin that exerts a potent inhibitory effect on the adenosinetri phosphatase activity of Escherichia coli BF1.
- This mycotoxin was isolated by Vleggaar et al. in the late 1970s and was given the name asteltoxin.
- On the basis of spectroscopic data and an X ray crystallographic analysis, these investigators were able to establish that structure and relative stereochemistry of asteltoxin.
- Asteltoxin is a trienic α-pyrone that bears a close structural relationship to aurovertin and citreoviridin, known inhibitors of oxidative phosphorylation.

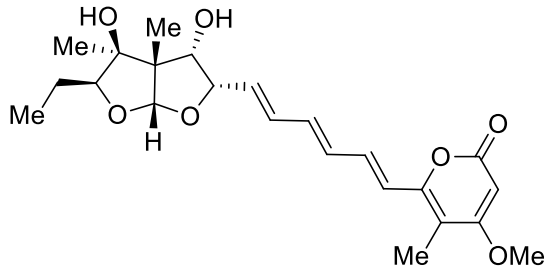


Aurovertin



Citreoviridin

a) Satre, M. *Biochem. Biophys. Res. Commun*. **1981** , *100*, 267. b) Kruger, G. J.; Steyn, P. S.; Vleggaar, R. *J. Chem. Soc., Chem. Commun*. **1979**, 441 . c) Mulheirn, L. J.; Beechey, R. B . ; Leworthy, D. P.; Osselton, M. D. *J. Chem. Soc., Chem. Commun*. **1974**, 874.

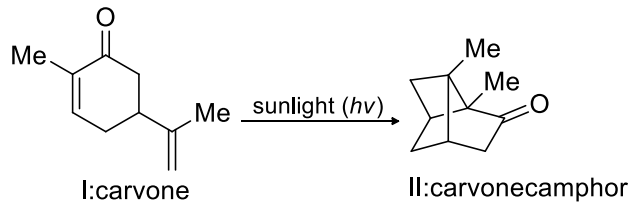


- The asteltoxin molecule is highly oxygenated and complex ; its dioxabicyclo[3.3.0]octane frame is distinguished by six contiguous stereogenic centers.

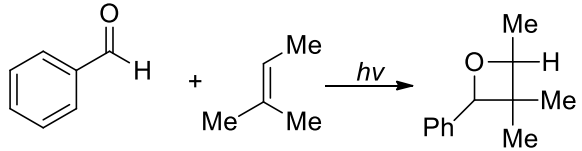
- Interestingly, it has been demonstrated that this highly oxygenated bicyclic substructure is responsible for the inhibition and binding properties of asteltoxin.

Sakabe, N.; Goto, T. ; Hirata, Y. *Tetrahedron Lett.* **1964**, 1825.

Representative [2+2] Photocycloaddition Reactions



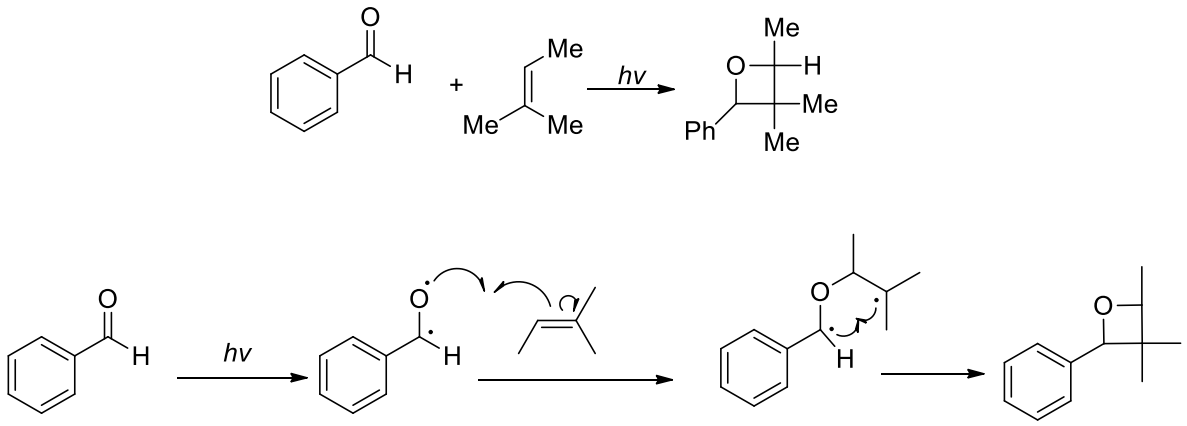
I:carvone II:carvonecamphor



III:benzaldehyde IV V

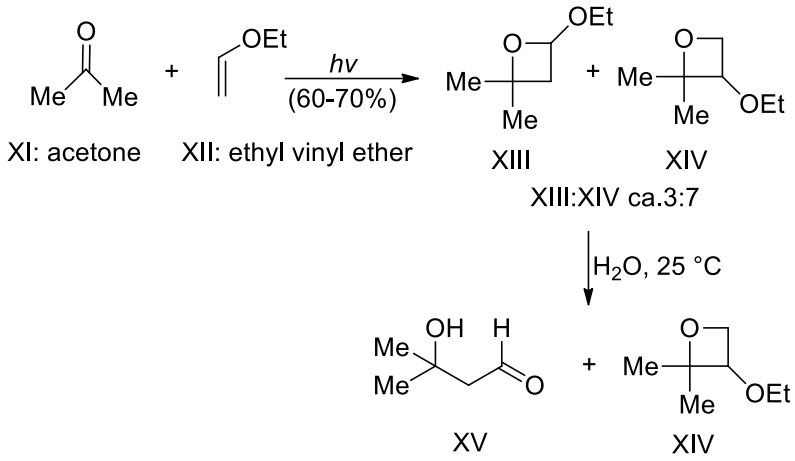
a) Ciamician, G.; Silber, P. *Ber. Dtsch. Chem. Ges*. **1908**, *41* , 1928.; b) Paterno, E.; Chieffi, G. *Gazz. Chim. Ital*. **1909**, *39*, 341.

Paterno-Buchi Reaction Mechanism



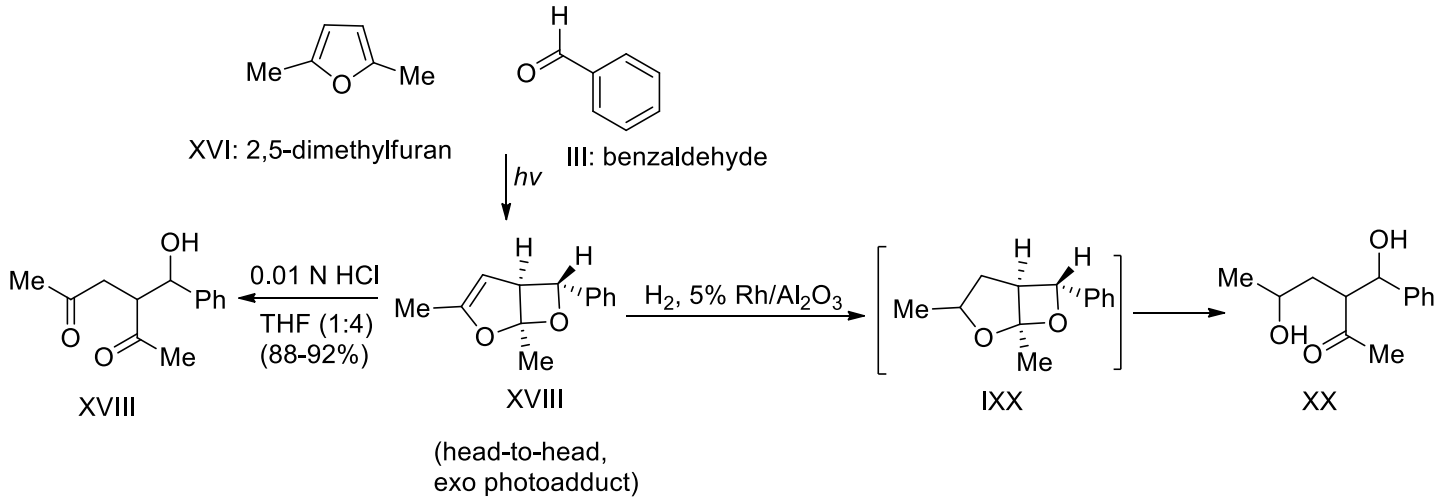
a) Ciamician, G.; Silber, P. *Ber. Dtsch. Chem. Ges*. **1908**, *41* , 1928.; b) Paterno, E.; Chieffi, G. *Gazz. Chim. Ital*. **1909**, *39*, 341.

Paterno-Buchi Reaction as a Photochemical Aldol Equivalent:



(a) Schroeter, S. H.; Orlando, C. M., Jr. *J. Org. Chem.* **1969**, *34*, 1181 ; (b) Schroeter, S. H. *J. Org. Chem.* **1969**, *34*, 1188.

Stereoselective Functionalizations of Furan-Aldehyde Photoadducts:



Woodward, R. B . ; Bader, F. E.; Bickel, H . ; Frey, A . J . ; Kierstead, R . W. *Tetrahedron* **1958**, *2*, 1 .

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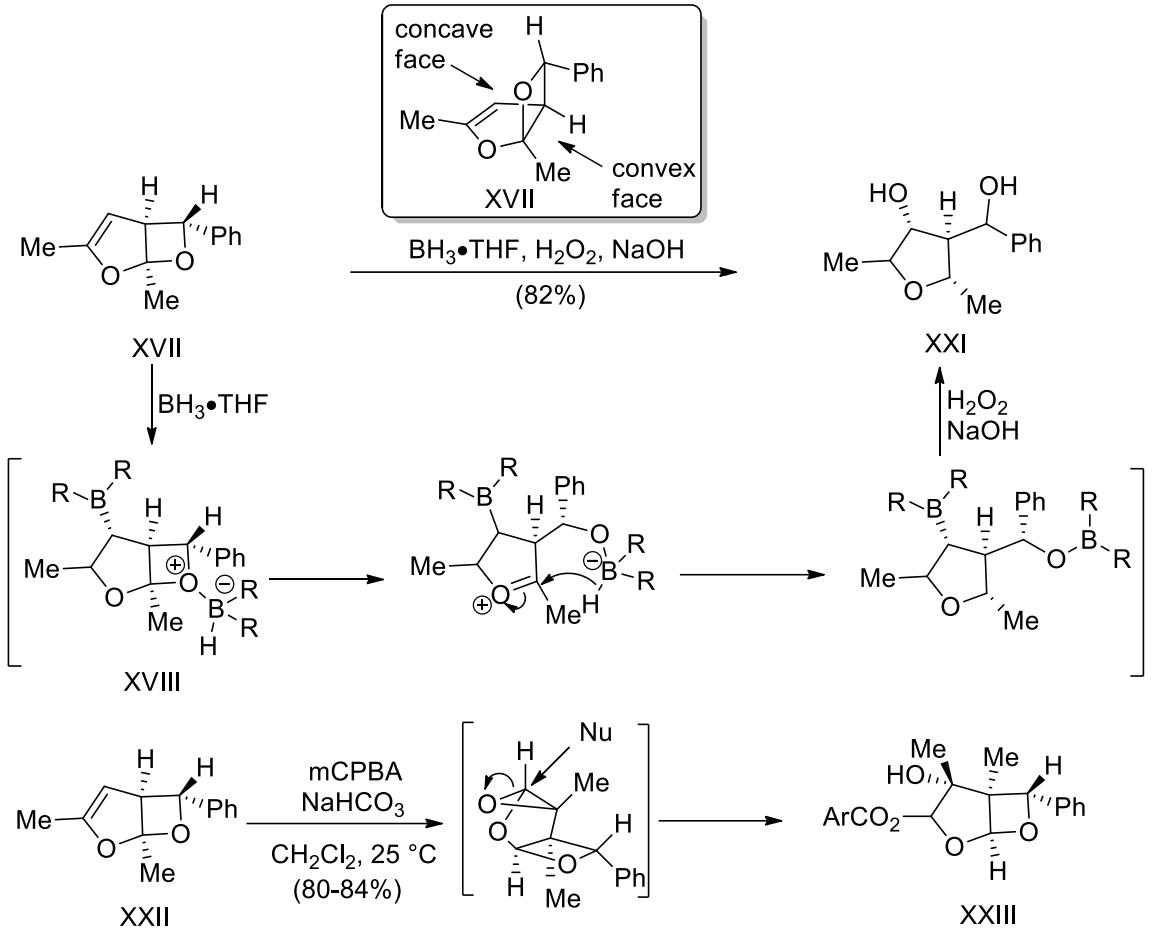
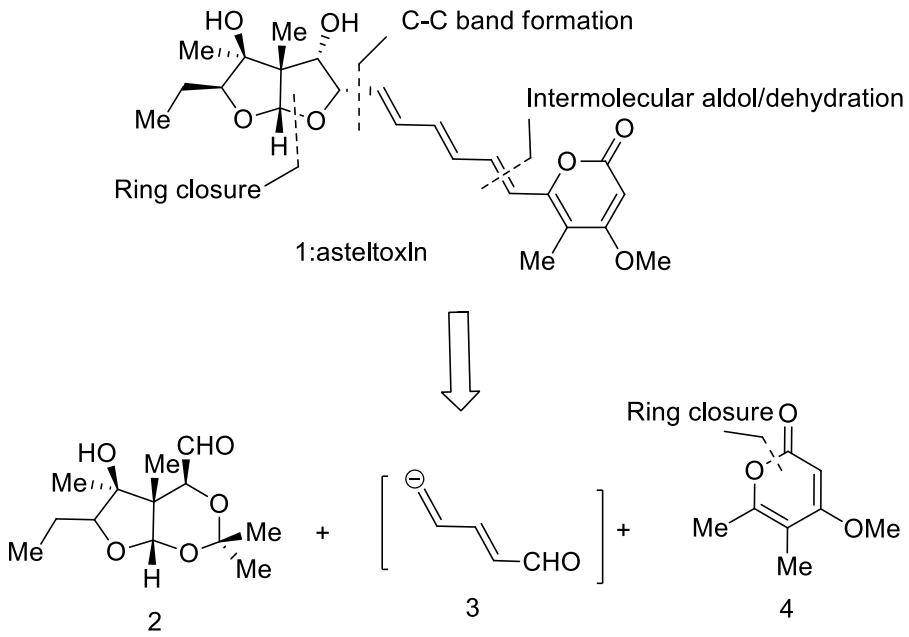
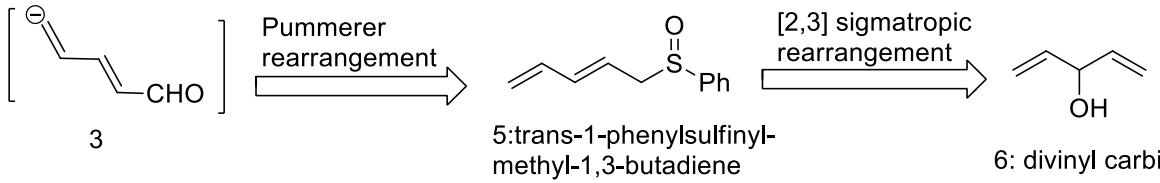


Woodward, R. B . ; Bader, F. E.; Bickel, H . ; Frey, A . J . ; Kierstead, R . W. *Tetrahedron* **1958**, *2*, 1 .

Retrosynthetic Analysis of Asteltoxin:



Retrosynthetic Analysis of 3:

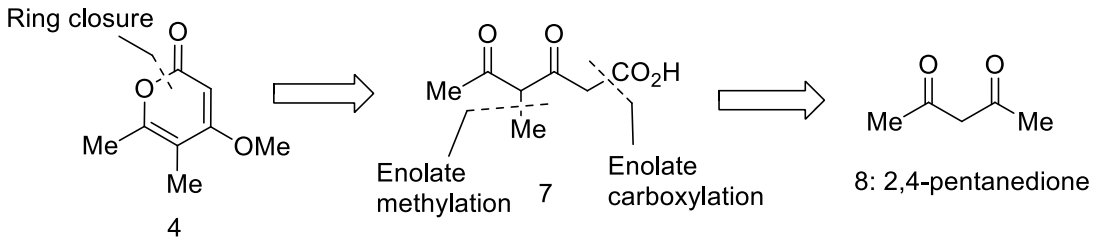


3

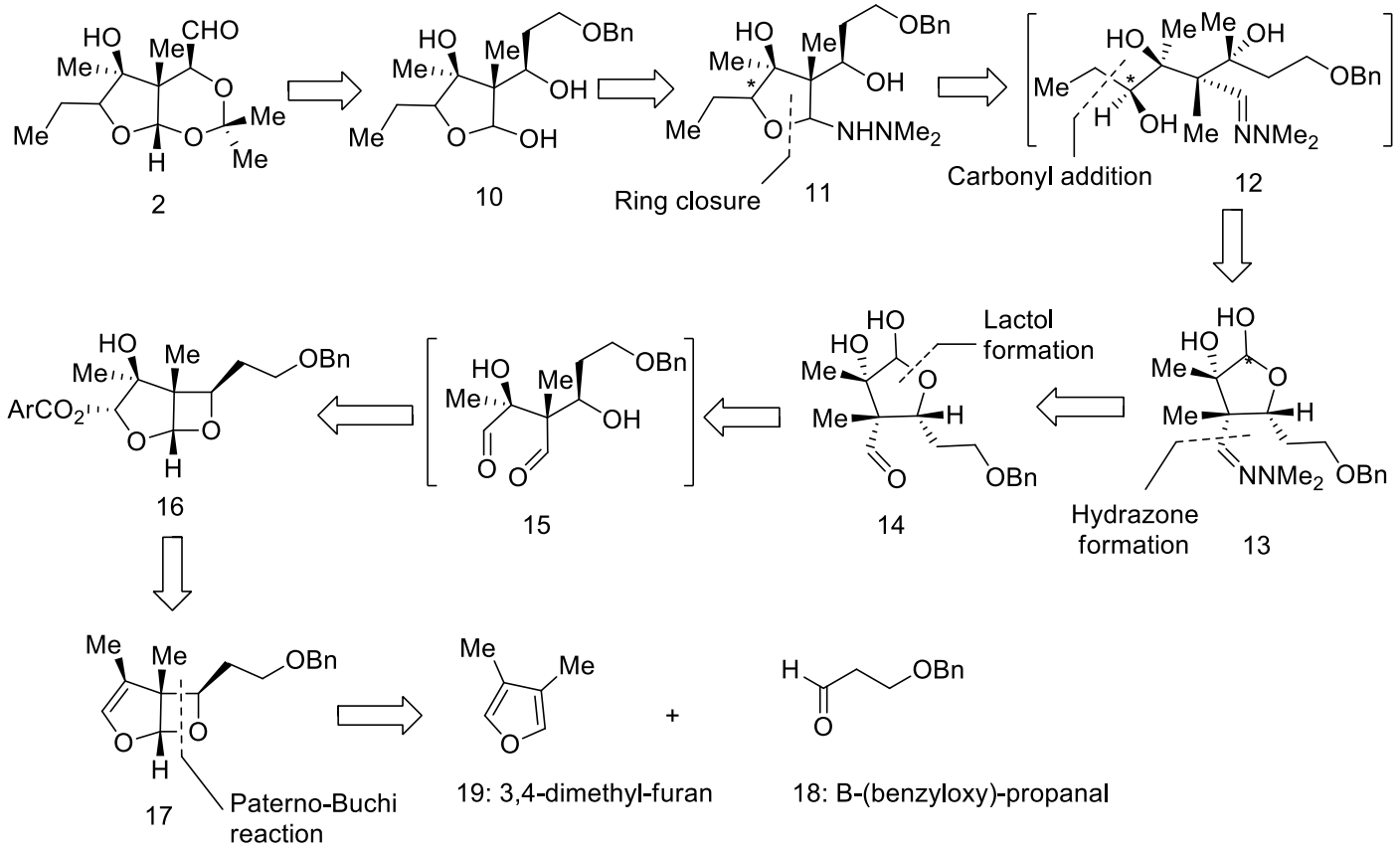
5:trans-1-phenylsulfinyl-methyl-1,3-butadiene

6: divinyl carbinol

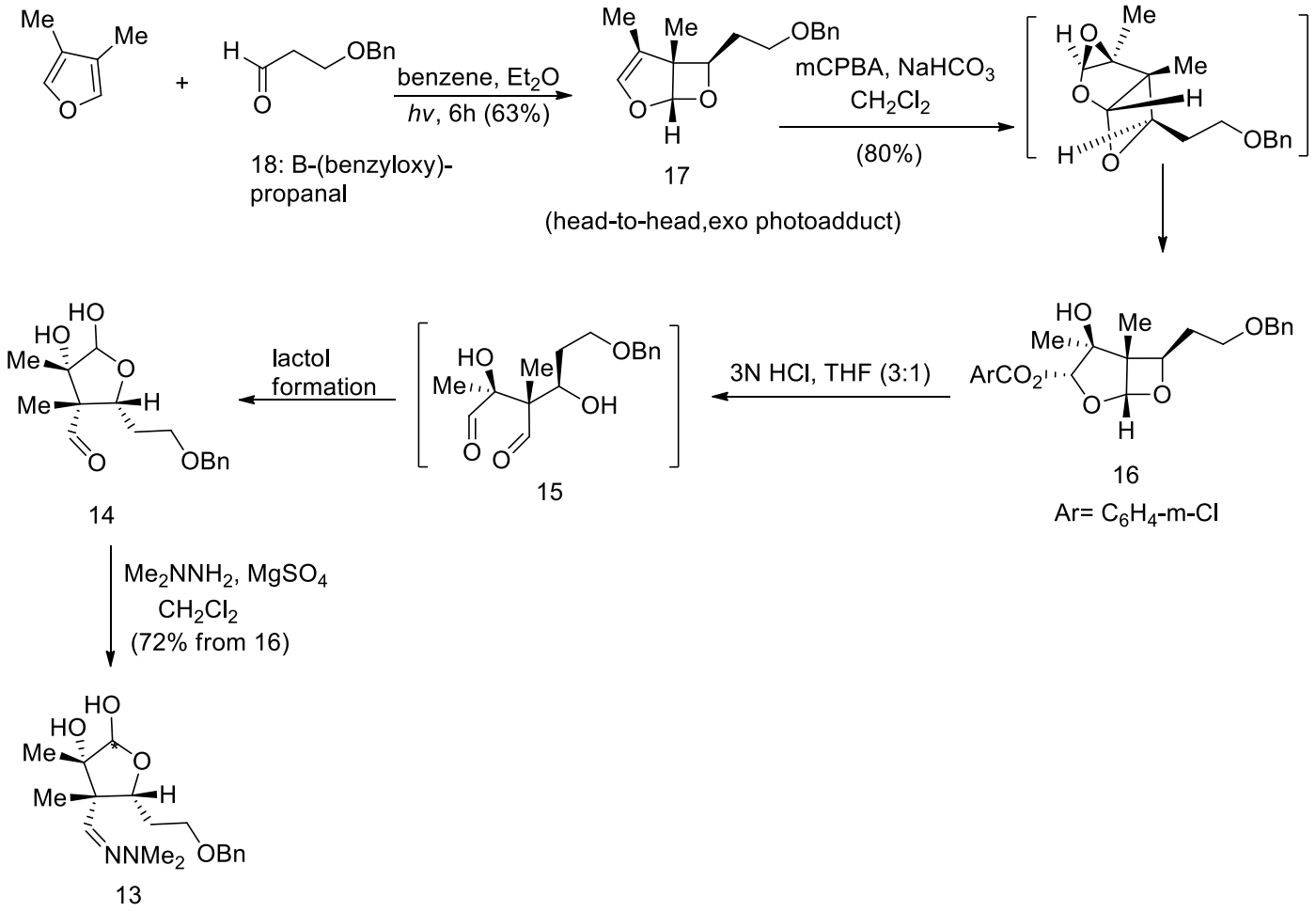
Retrosynthetic Analysis of 4:



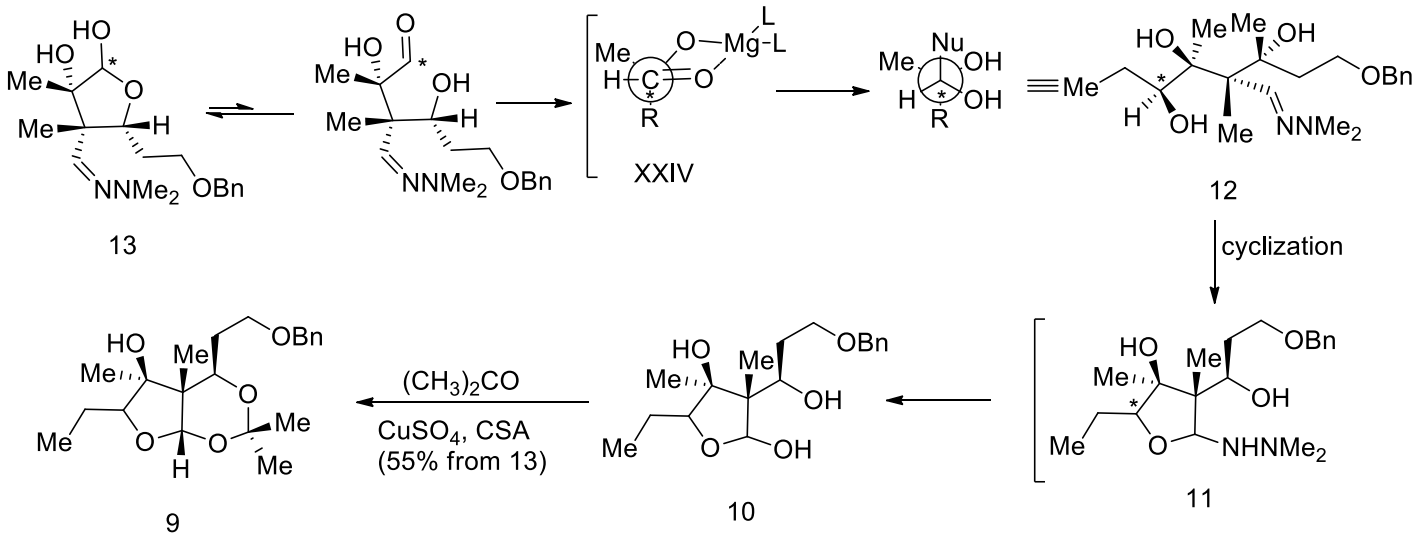
Retrosynthetic Analysis of 2:



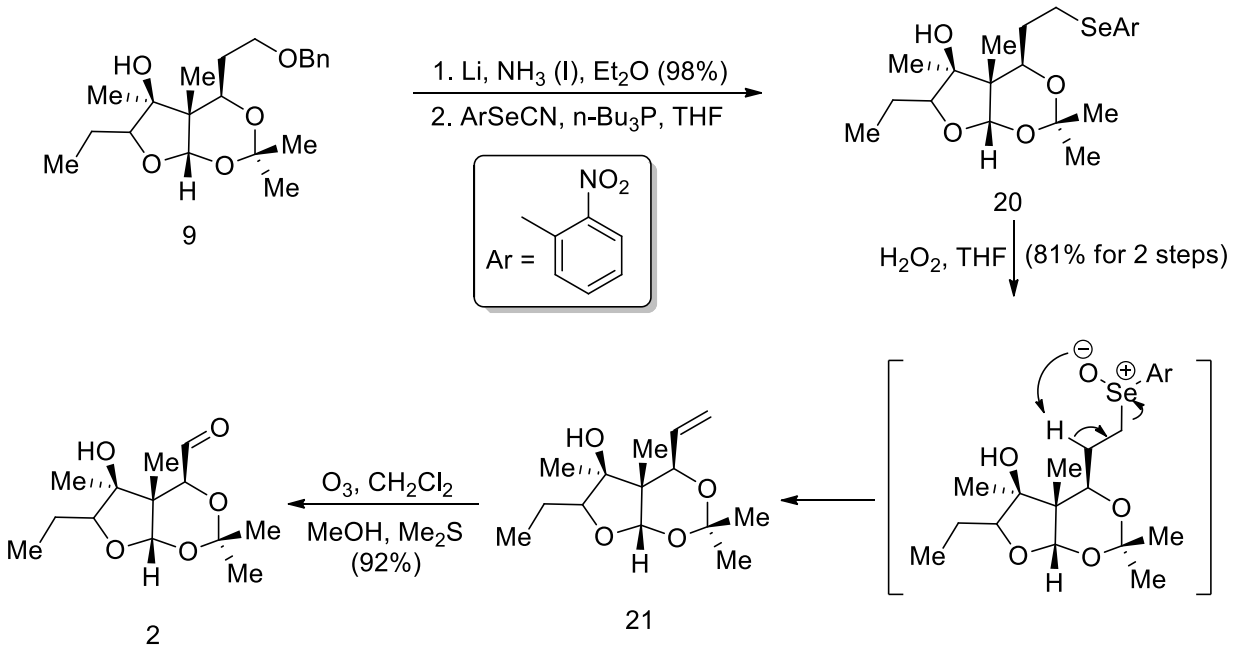
Synthesis of Intermediate 9:



Synthesis of Intermediate 9:



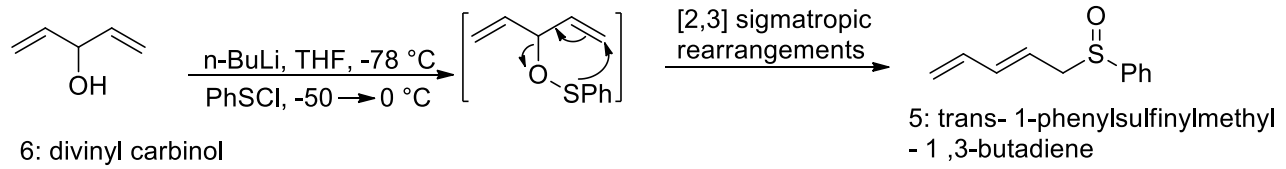
Synthesis of Intermediates 2:



Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.

Synthesis of Intermediates 5 (b), and 4 (c):

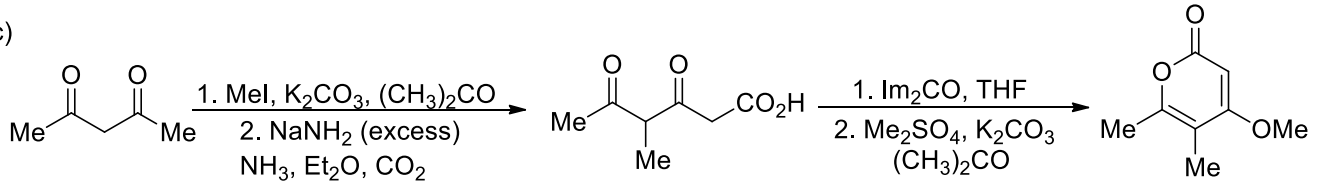
b)



6: divinyl carbinol

5: trans- 1-phenylsulfinylmethyl - 1 ,3-butadiene

c)



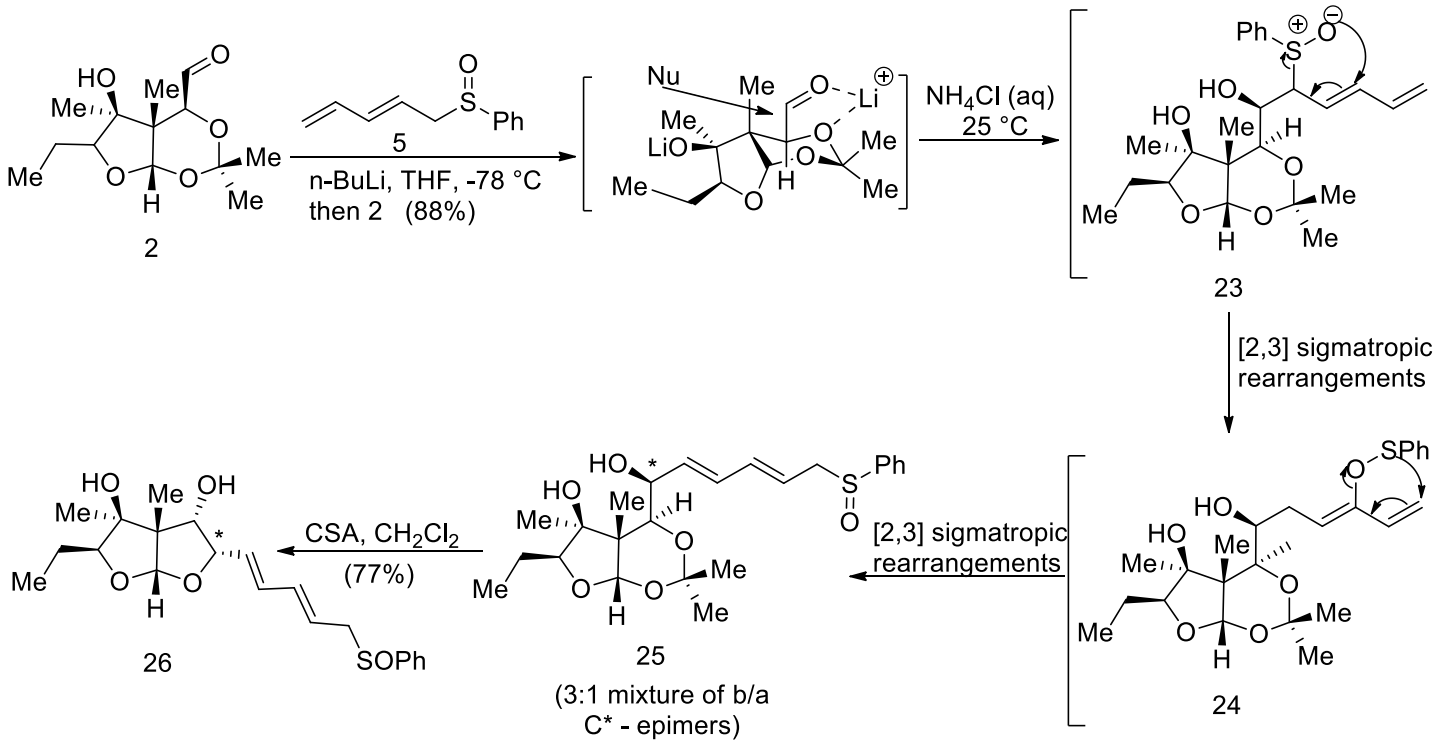
8: 2,4 pentanedione

7

4

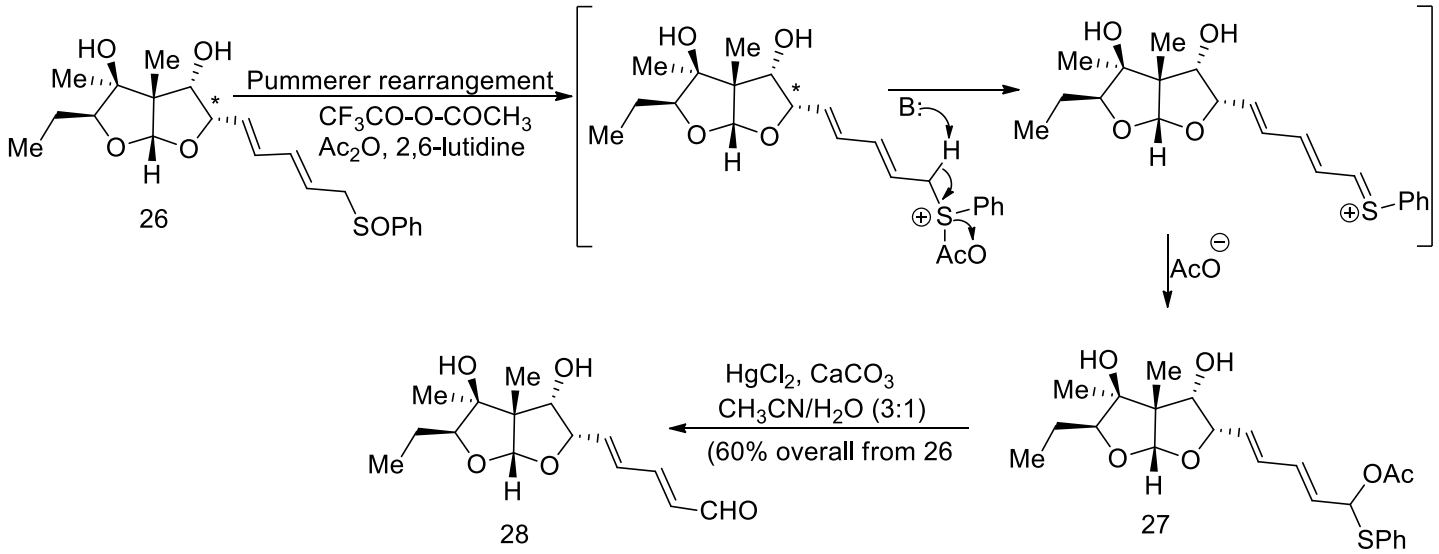
Evans, D. A . ; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147.

Synthesis of Intermediate 28:



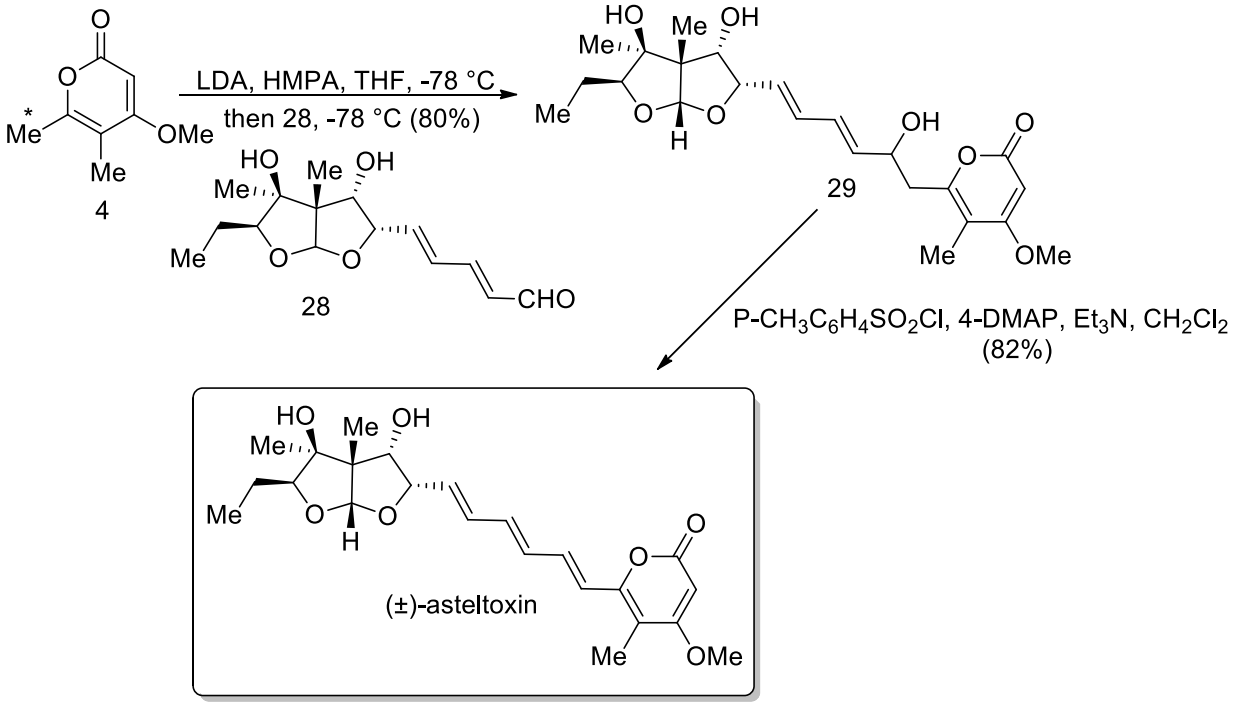
(a) De Lucchi, O.; Miotti, U . ; Modena, G. *Org. React. (N. Y.)* **1991**, *40*, 157; (b) Moiseenkov, A. M.; Dragan, V. A.; Veselovskii, V. V. *Russ. Chem. Rev. (Engl. Transl.)* **1991**, *60*, 643.

Synthesis of Intermediate 28:



(a) De Lucchi, O.; Miotti, U . ; Modena, G. *Org. React. (N. Y.)* **1991**, *40*, 1 57; (b) Moiseenkov, A. M.; Dragan, V. A.; Veselovskii, V. V. *Russ. Chem. Rev. (Engl. Transl.)* **1991**, *60*, 643.

Synthesis of (±)-Asteltoxin:



Conclusion:

- Since its discovery in 1909, the process now known as the Paterno-Büchi reaction has evolved into a powerful tool for the elaboration of highly oxygenated and stereochemically complex molecules.

- The relationship of the Paterno-Büchi reaction to the classic aldol condensation is particularly interesting. In certain circumstances, it can provide access to p-hydroxy carbonyl compounds that could not be efficiently prepared through a direct aldol condensation.

- Schreiber and his colleagues dramatically extended the utility of furan-aldehyde Pateno- Büchi reactions for the synthesis of complex natural products.

- The photo-induced union of simple, achiral furans and aldehydes furnishes a dioxabicyclo [3.2.0Jheptene photoadduct that can serve as a valuable template for the creation of stereogenic centers.

- The folded or cup-shaped molecular frameworks of these photoadducts are distinguished by a convex face and a considerably more hindered concave face that permit highly diastereoselective operations to be carried out on the remaining site of unsaturation.

- The most impressive feature of Schreiber's synthesis of asteltoxin is the speed with which vicinal stereochemical relationships are secured, in short order, through a sequence of reactions in which the furan aldehyde Paterno- Büchi photocycloaddition plays a commanding role.

THANK YOU FOR YOUR ATTENTION