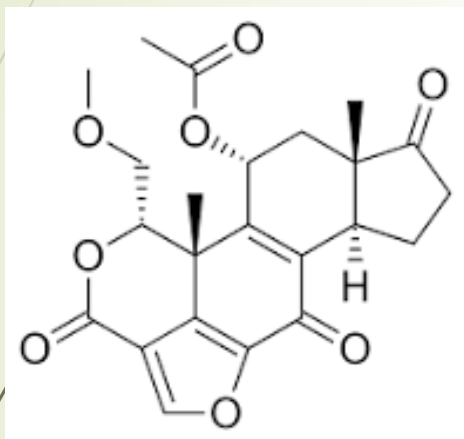


Wortmannin Total Synthesis

Aria Vahdani



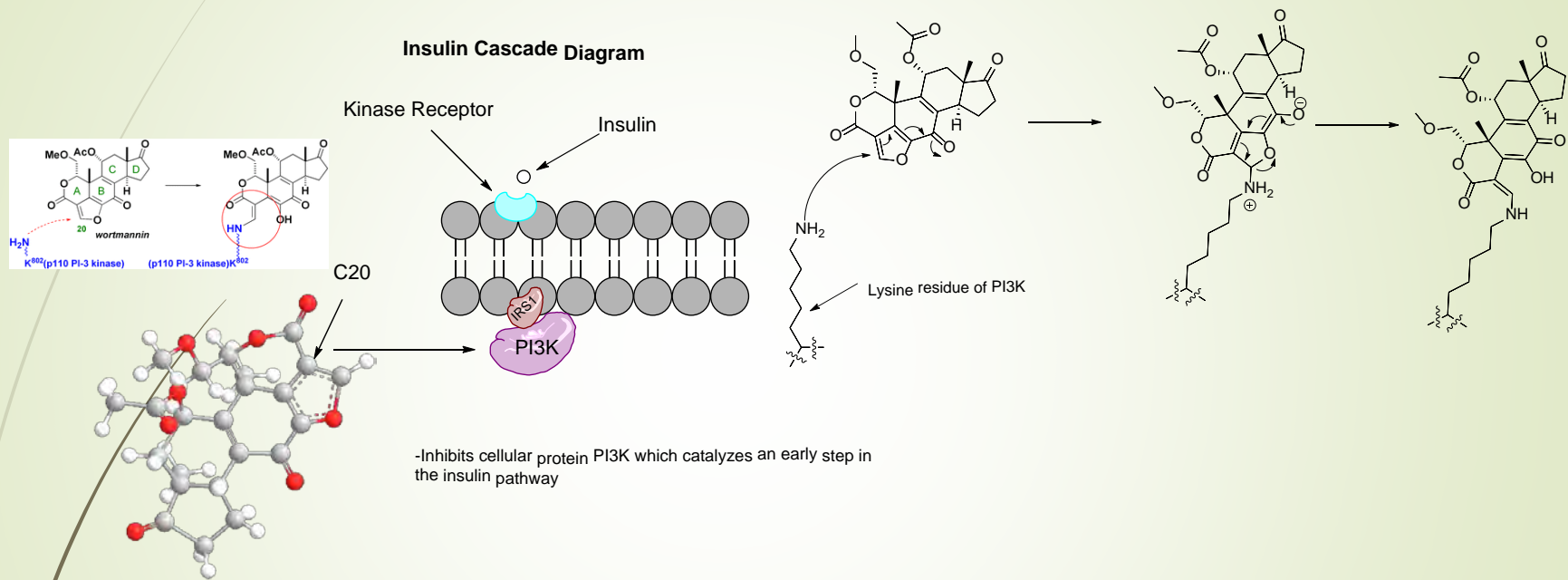
Penicillium funiculosum and/or *Fusarium moniliforme*



Background . .

- A fungal steroidal metabolite with anti-inflammatory properties originating in the *penicillium funiculosum* plant pathogen which infects pineapples.
- Later identified as a potent PI3K (phosphoinositide 3-kinase) inhibitor, which falls into a category of anti-cancer drugs being actively investigated for treatment
- Some adverse side effects include irreversible memory loss and impaired spatial learning abilities.

Biochemical Activity of Wortmannin

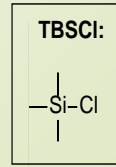
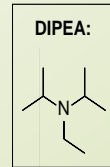
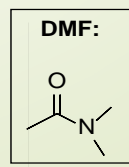
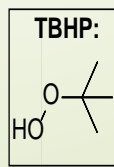
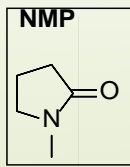
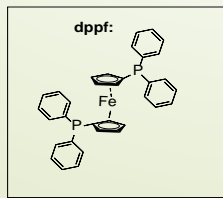
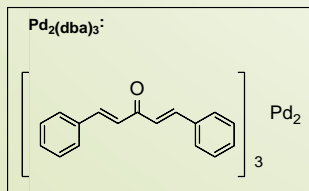
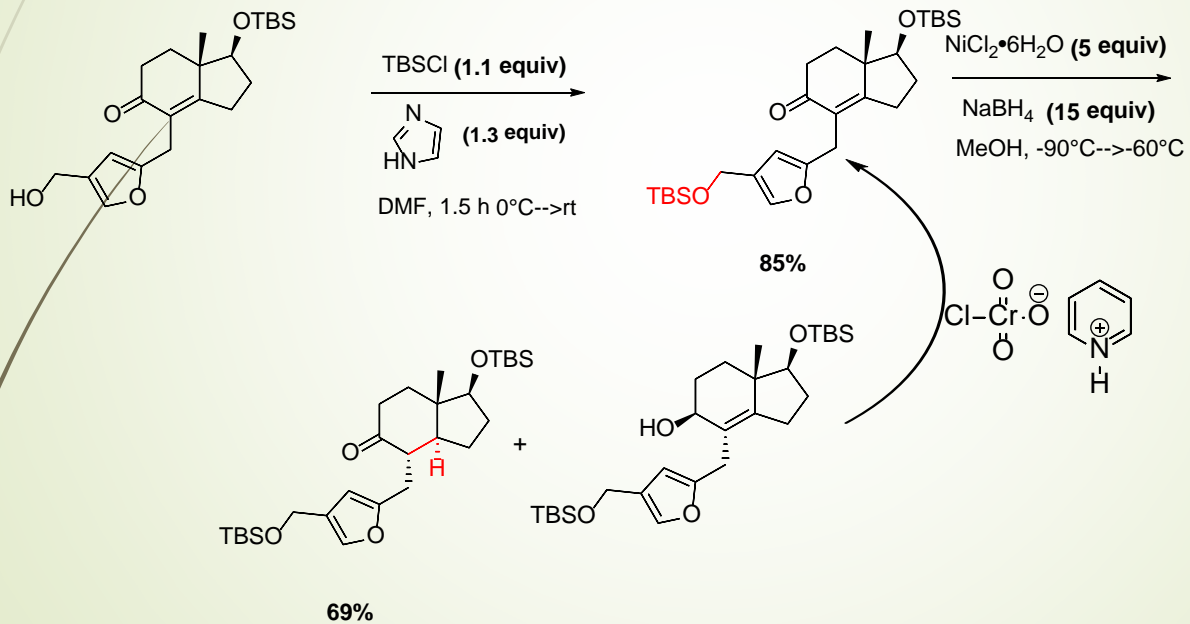
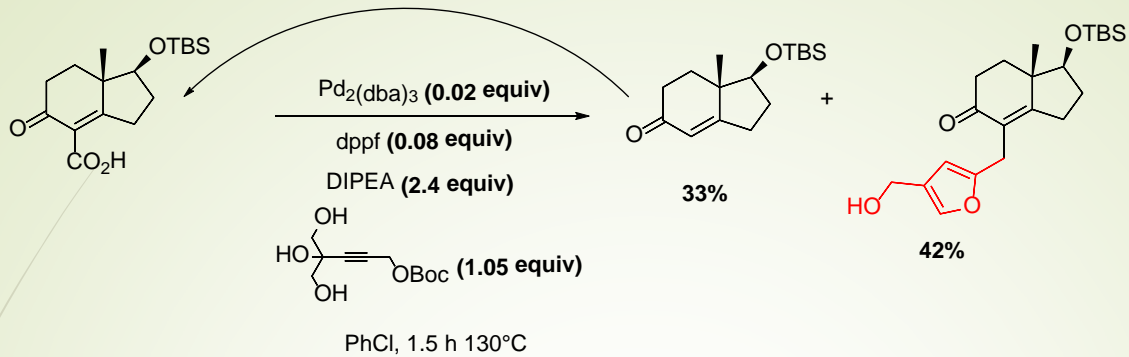


-Wortmannin was administered to inhibit PI3K in order to study and pinpoint the source of brain enlargement and rare seizures in mice, as a result of abnormalities in this pathway.

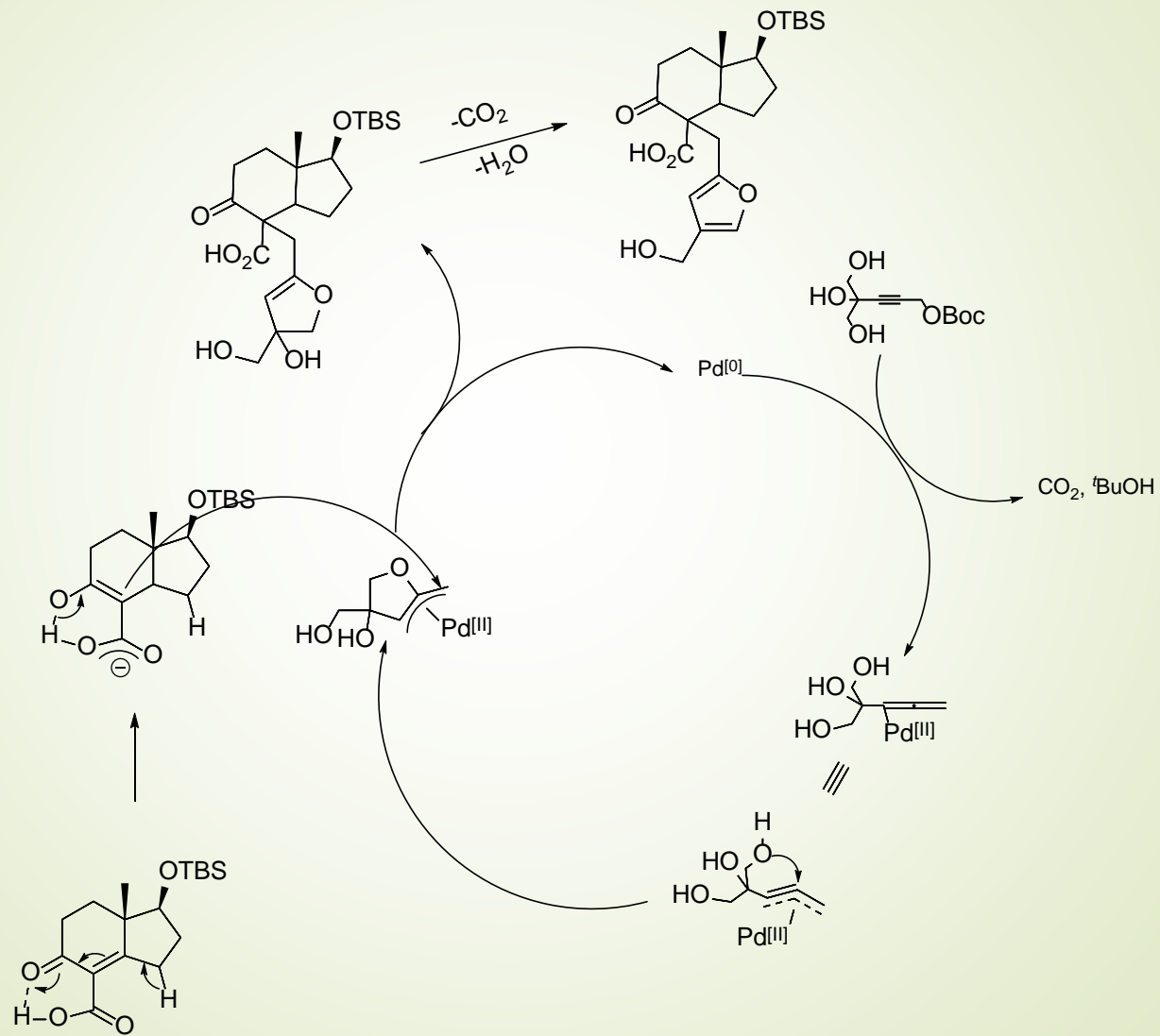
-Results showed that wortmannin did indeed decrease brain in this signaling pathway, and ultimately a reduction in brain size after a short time after oral administration

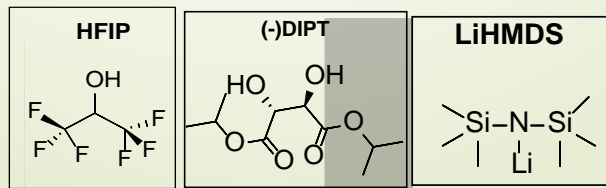
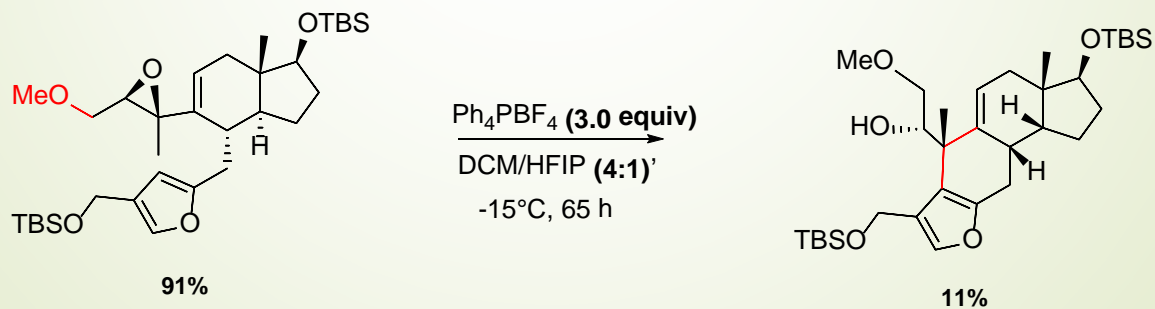
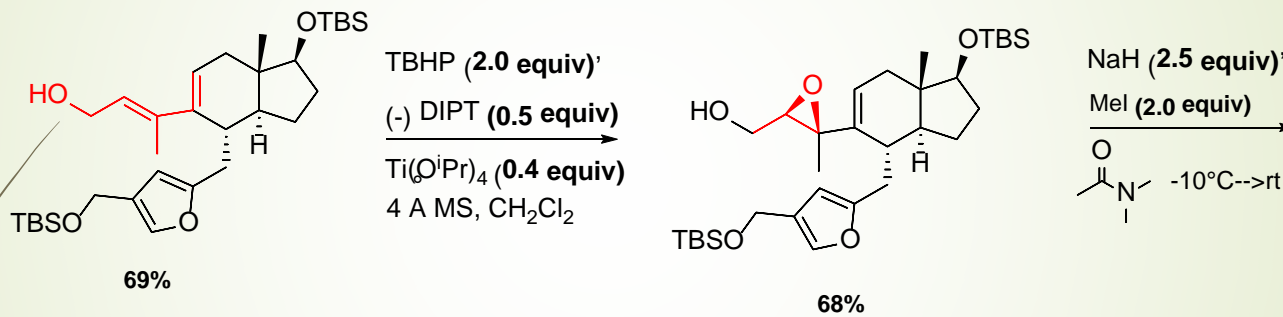
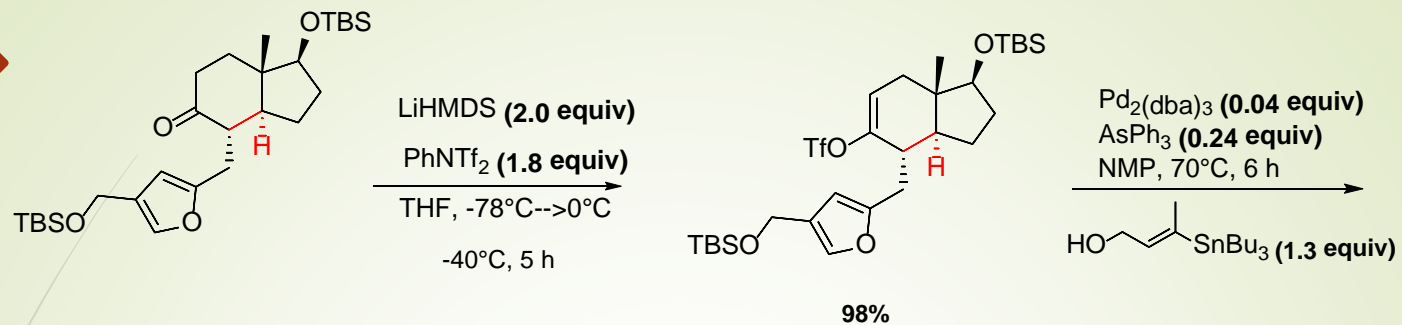
Wipf, P.; Halter, R. J. *ChemInform* **2005**, 36 (39).

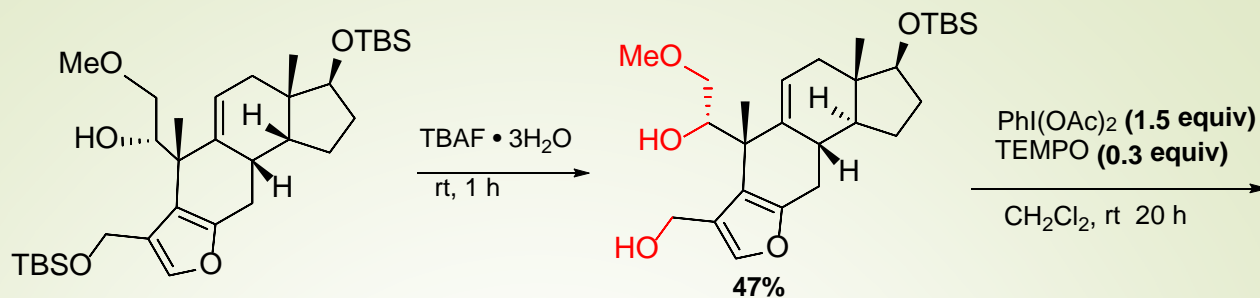
Mackay, K. B.; Lowenson, J.D.; Clarke, S. G. *PLOS ONE* **2012**, 7 (10)



Palladium Catalyzed Cycle for Connecting Hajos-Parrish Ketone Derivative to the Desired Furan Moiety

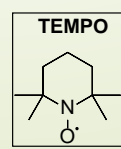
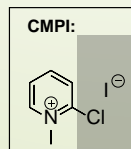
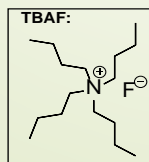
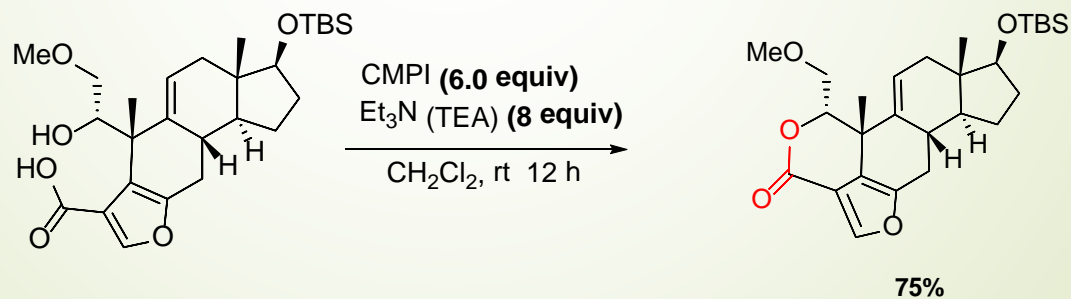
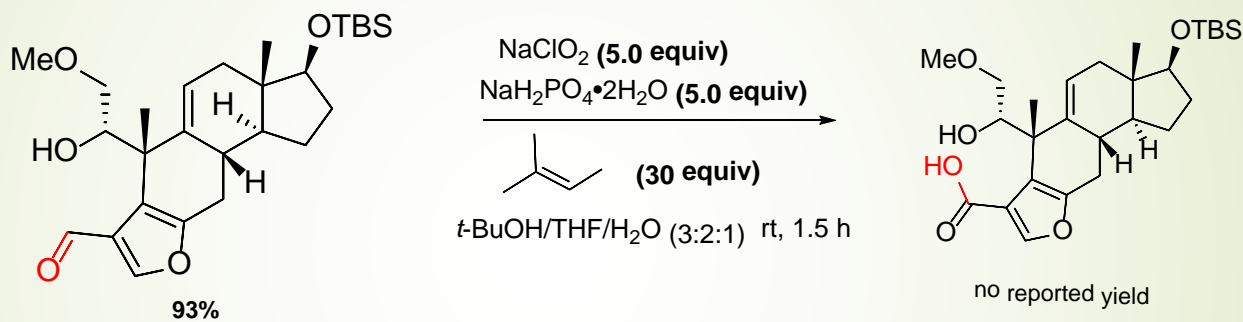




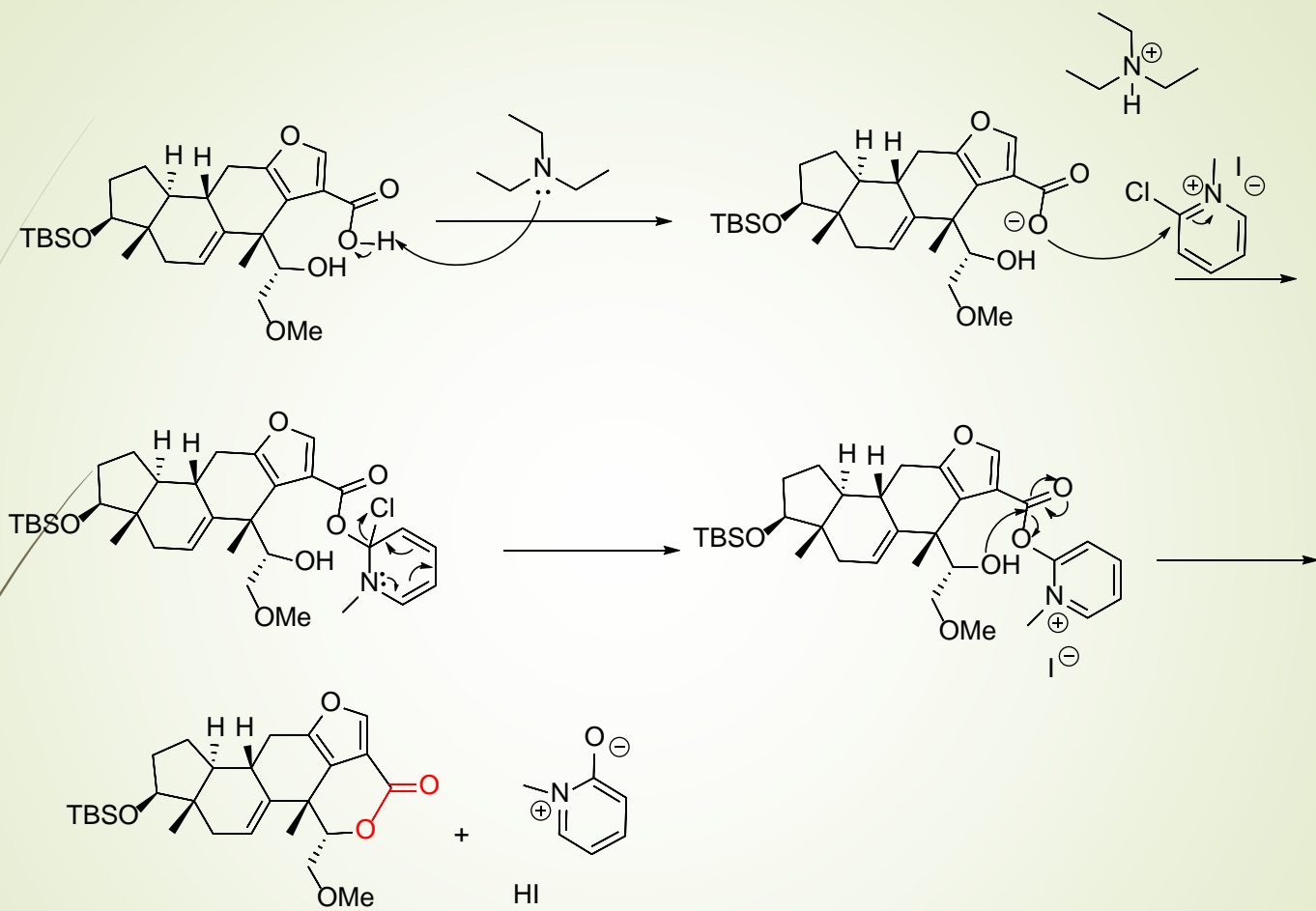


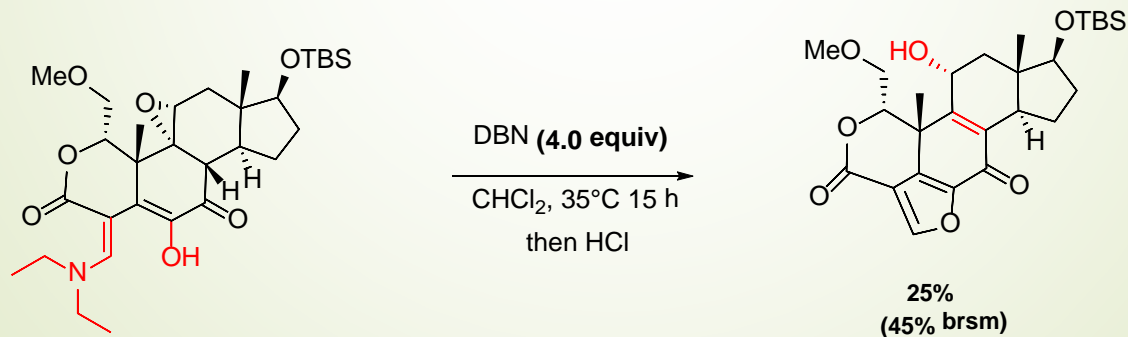
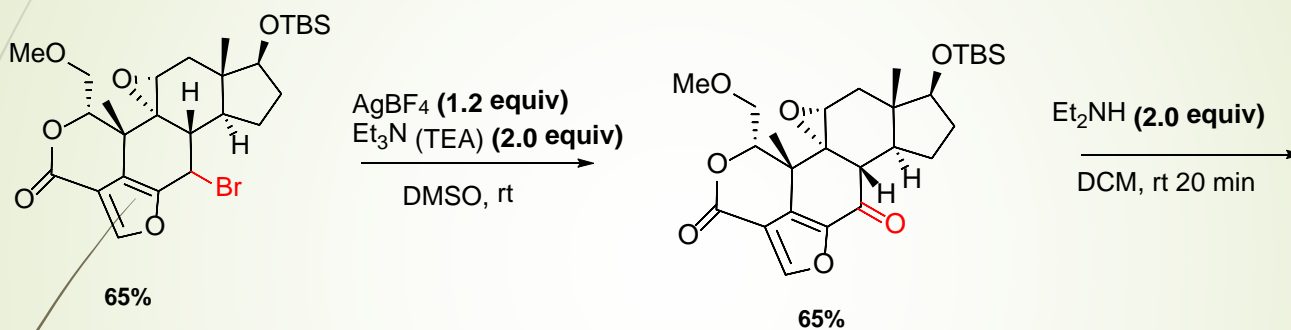
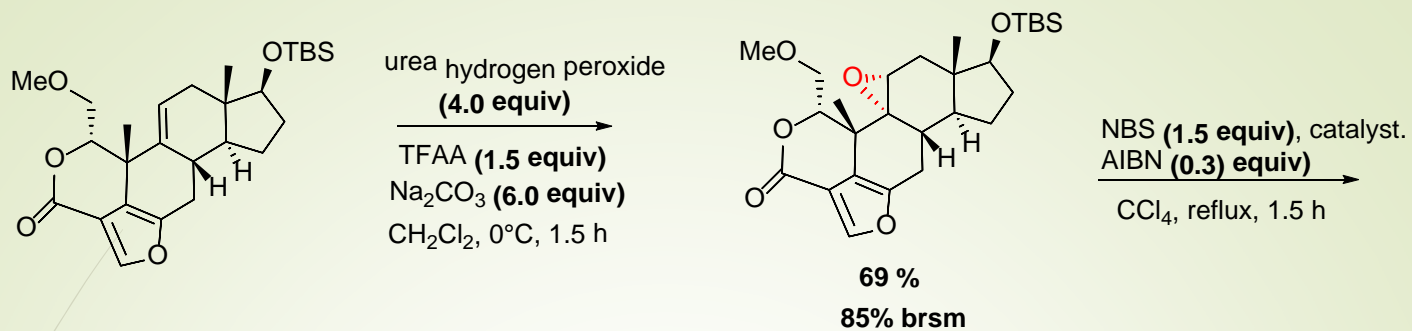
PhI(OAc)₂ (1.5 equiv)
 TEMPO (0.3 equiv)

CH₂Cl₂, rt 20 h

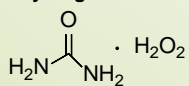


Mukaiyama Condensation Mechanism

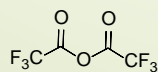




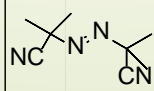
Urea/Hydrogen peroxide



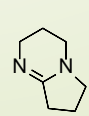
TFAA



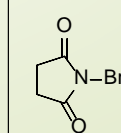
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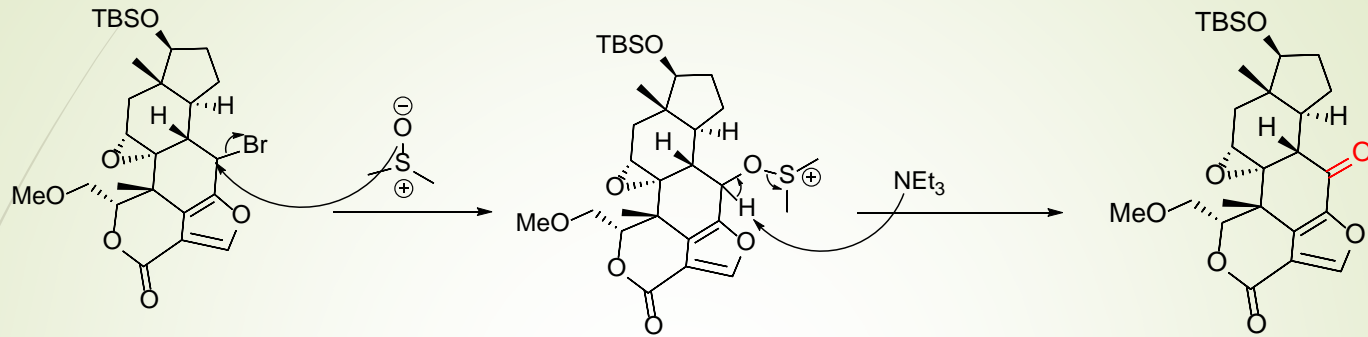
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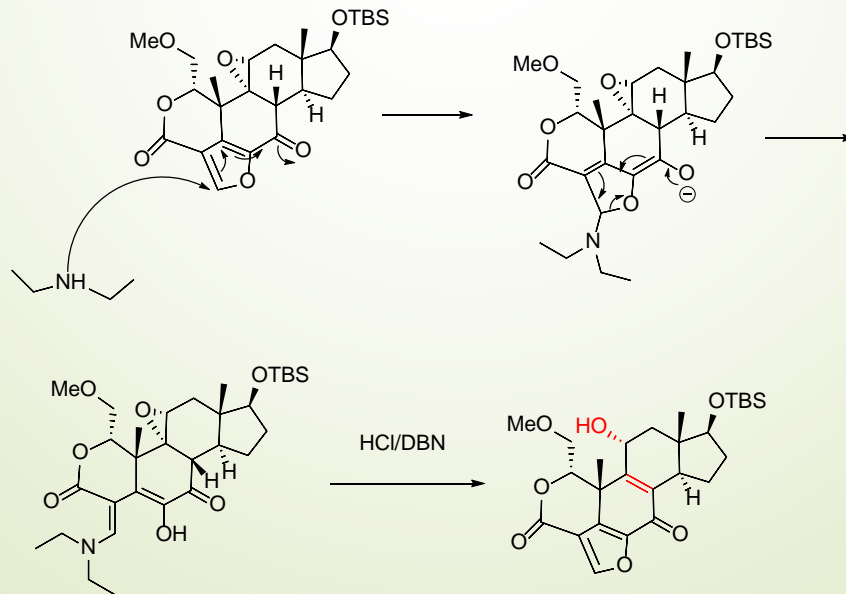
NBS



Kornblum Oxidation Mechanism



Using NHEt_2 and DBU Elimination to form $\alpha\beta$ Unsaturated Moiety From Kornblum Oxidation Product



Wohl Ziegler Reaction Mechanism to Allylic Bromination

