An Accelerated Intermolecular Rauhut-Currier Reaction Enables the (–)-Flueggenine C

Jeon, S.; Han, S. *J. Am Chem. Soc*, **2017**, *139*, 6302–6305.

Securinega alkaloids consisting of more than 70 natural products and are known since 1956

Recent isolation of bioactive natural products from Flueggea virosa enabled the isolation of various dimeric and oligomeric alkaloids expanding its structural repertoire

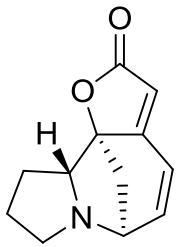
The biosynthesis of compounds **4** and **5** was reported using a self-catalyzed Baylis-Hilman reaction

flueggenine A (**4**) showed modest cytotoxicity against the P-388 tumor cell line

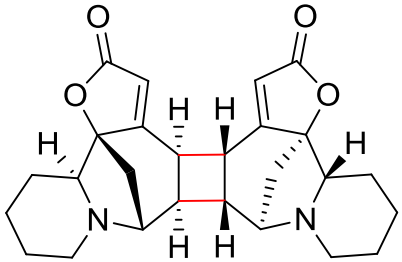
Flueggenine D and fluevirosinine B exhibited promising anti-HIV activities

The first asymmetric total synthesis of flueggenine C (**6**), a C,C-linked dimeric securinega Alkaloid was achieved in this work.

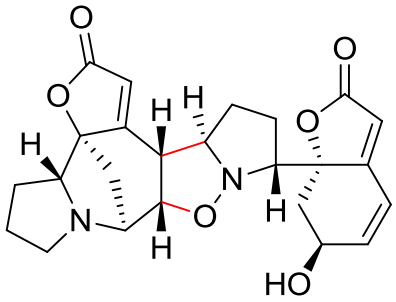
Natural products containing the DMOA (1) core



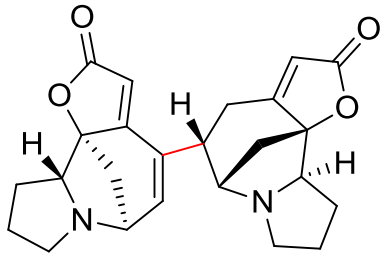
norsecurinine (**1**)



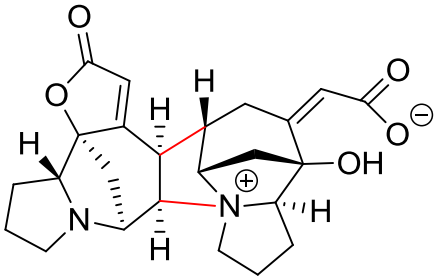
flueggedine (**2**)



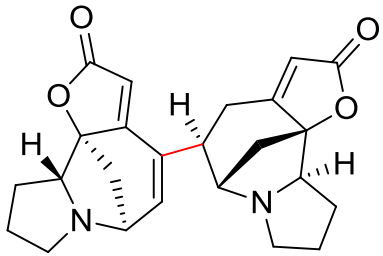
flueggine A (**3**)



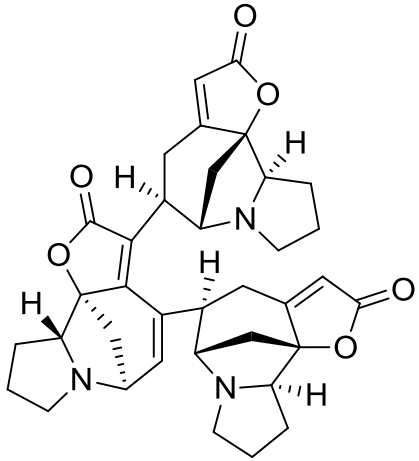
flueggenine A (**4**)



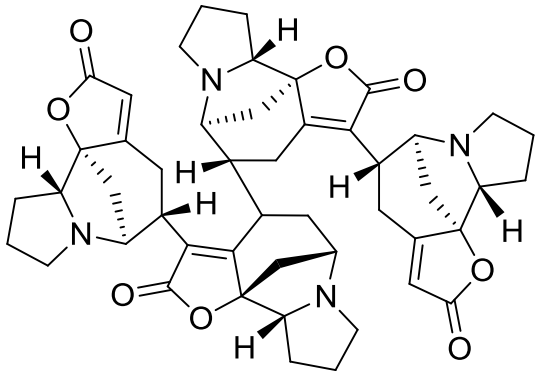
flueggenine B (**5**)



flueggenine A (**4**)



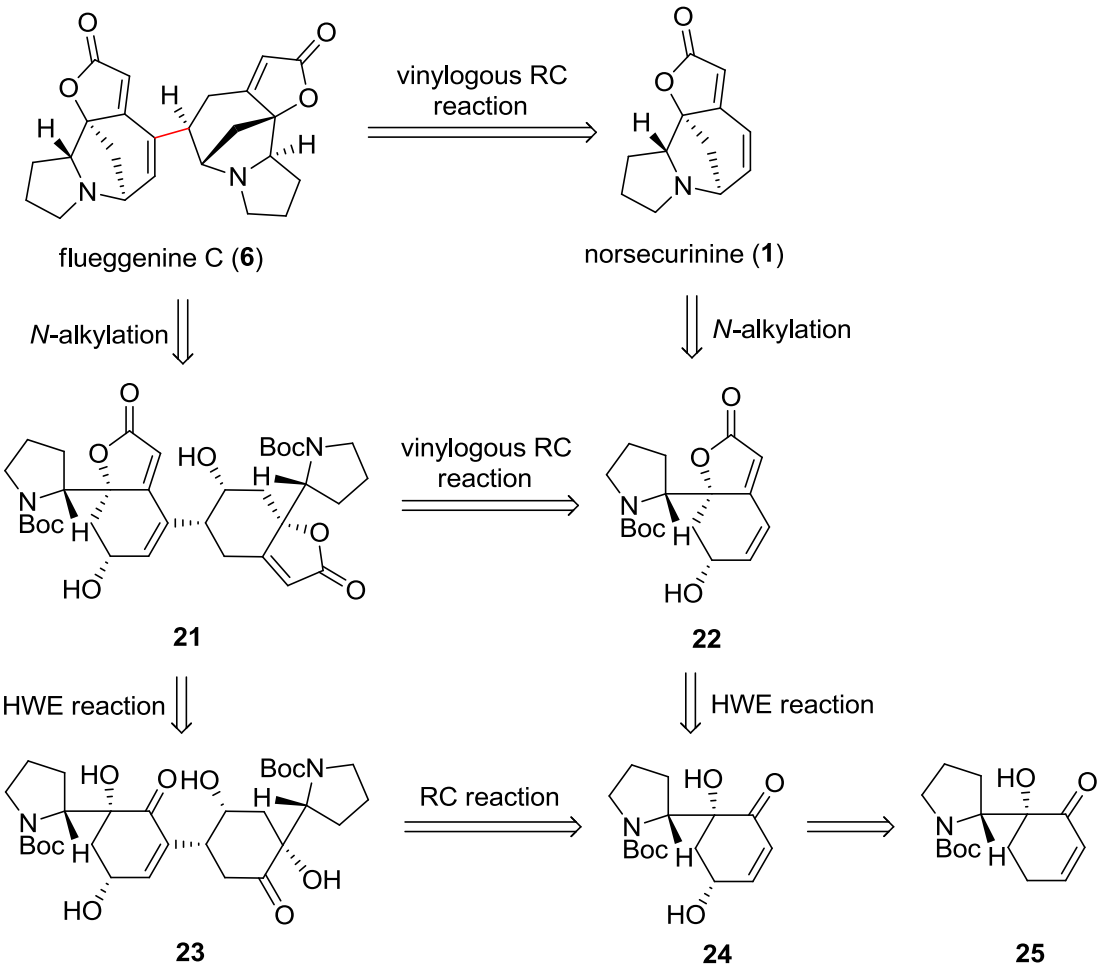
fluevirosine D (**7**)



fluevirosine D (**7**)

Monomeric, dimeric and oligomeric alkaloids

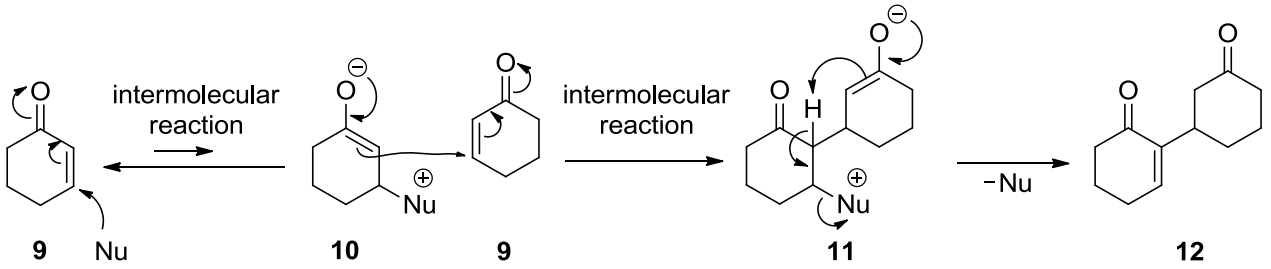
Retrosynthetic Analysis of Flueggenine C (6)



RC reaction forms a C−C bond between two Michael acceptors in the presence of a nucleophilic catalyst

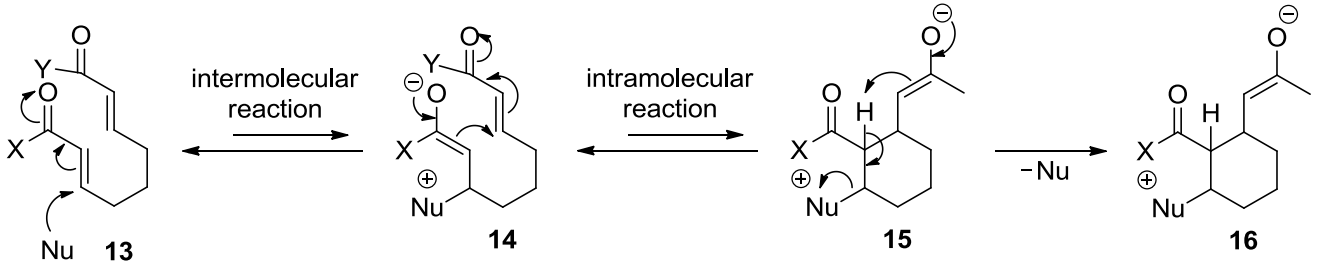
Possible modes of reactivity in Rauhut-Currier reactions

Conventional Intermolecular RC Reaction



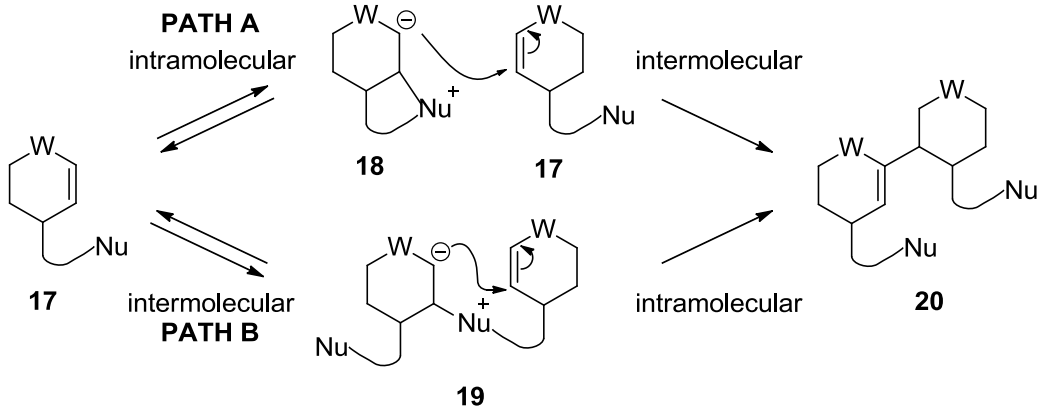
Low reactivity

Intramolecular RC Reaction



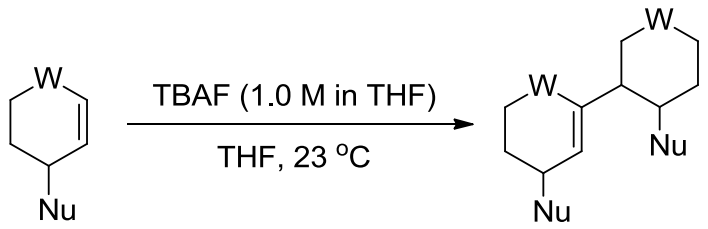
High reactivity

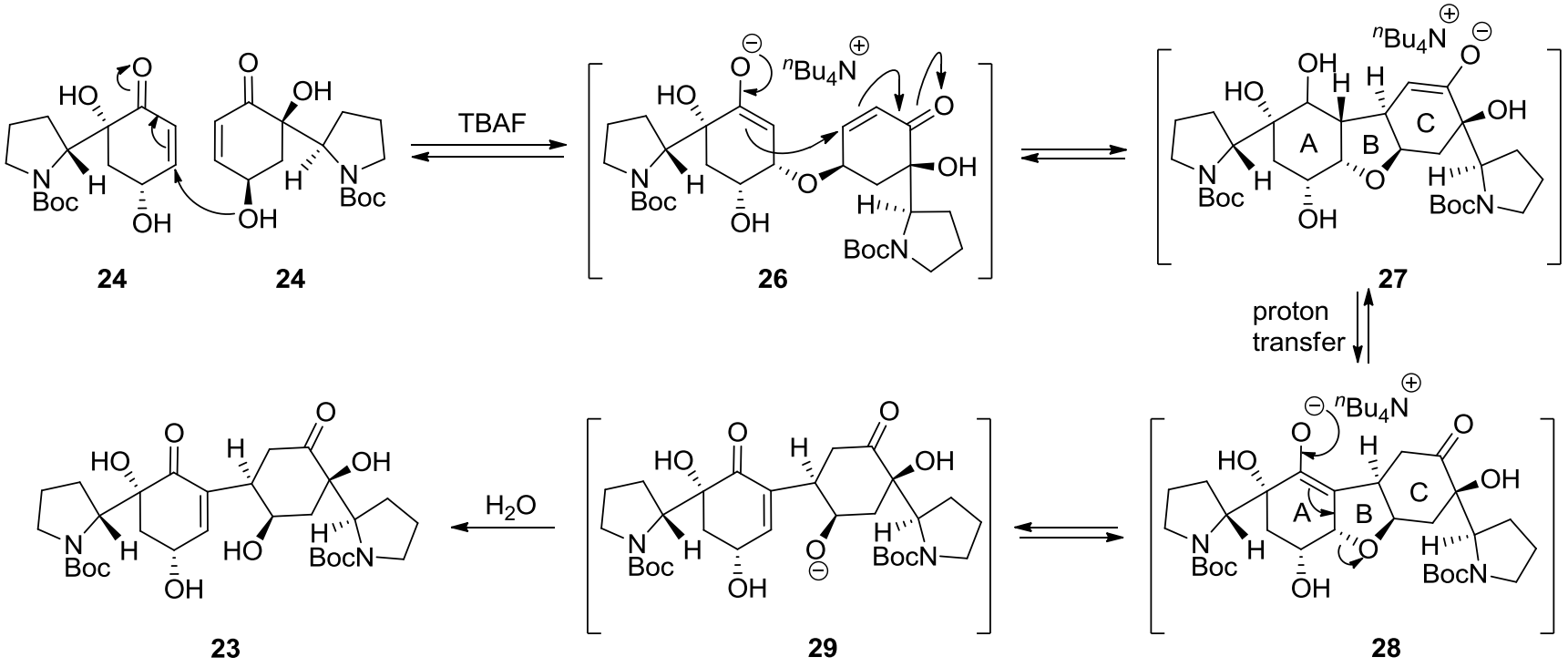
Accelerated Intermolecular RC Reaction (proposed)



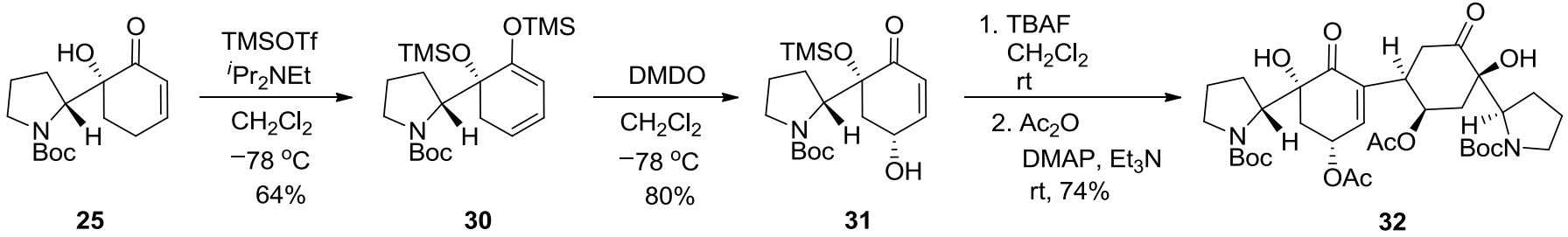
High reactivity

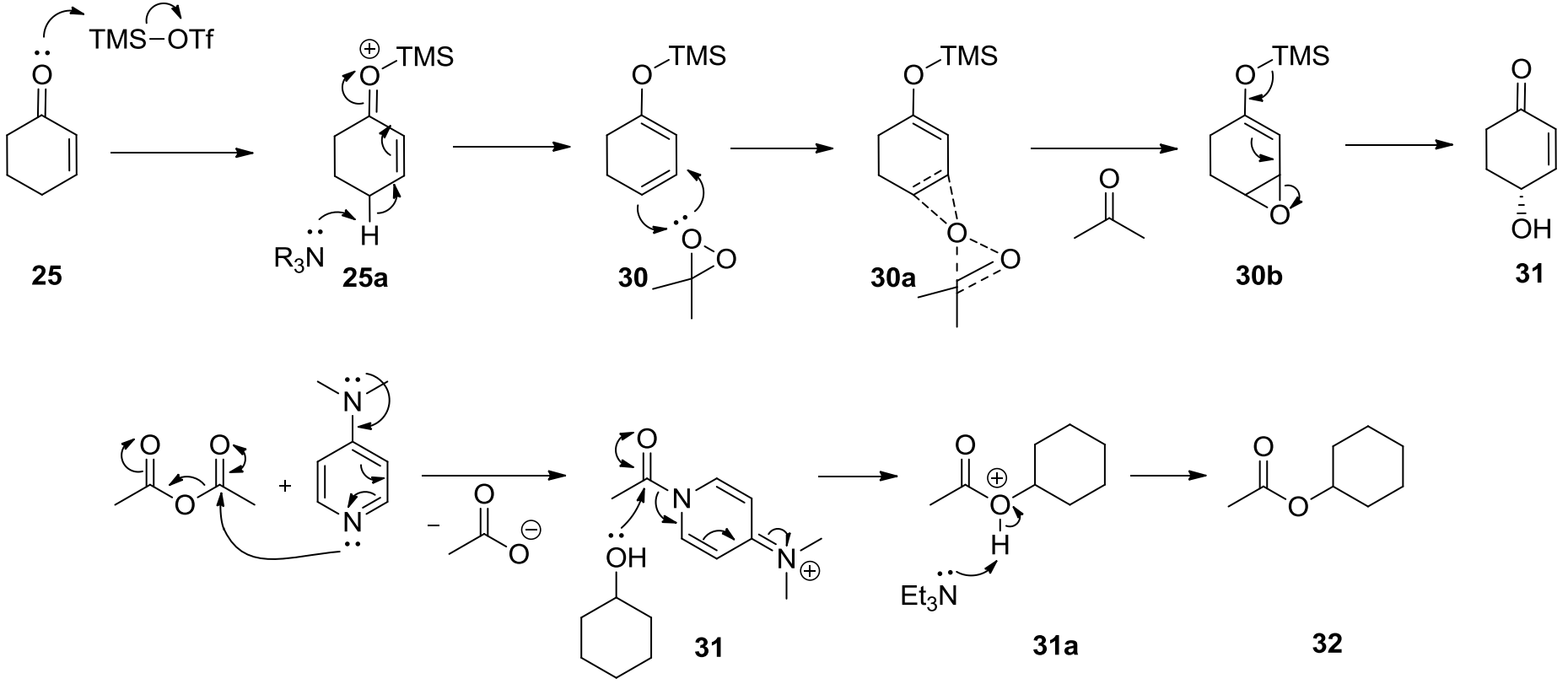
Accelerated RC reaction of enone 24



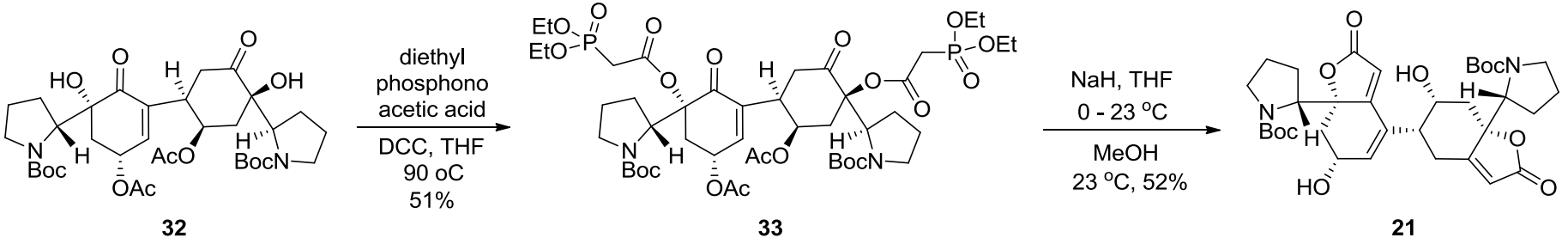


Mechanistic explanation

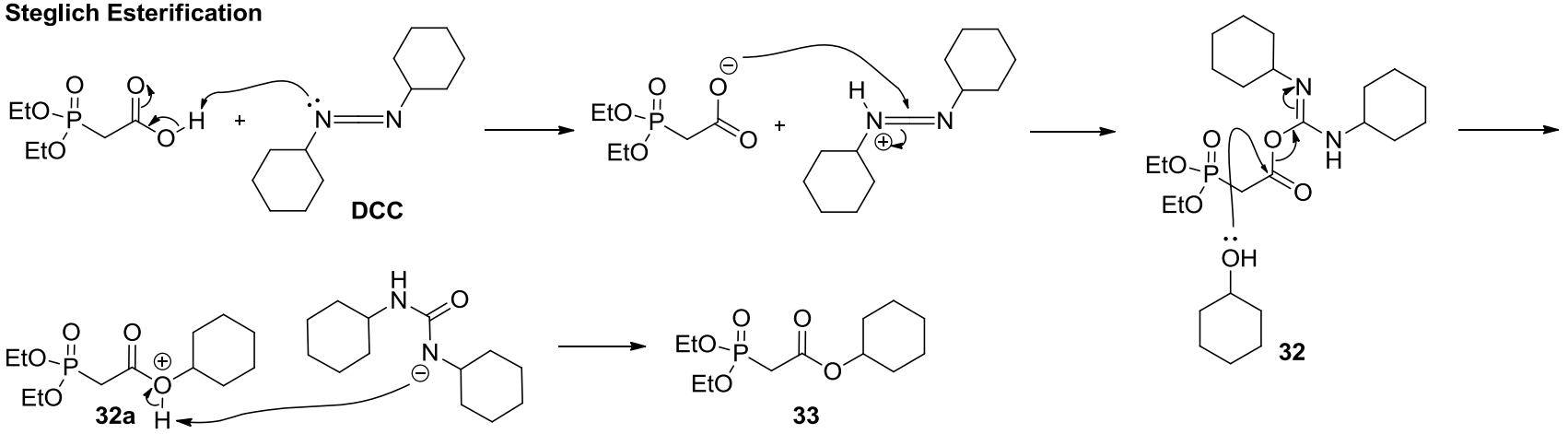




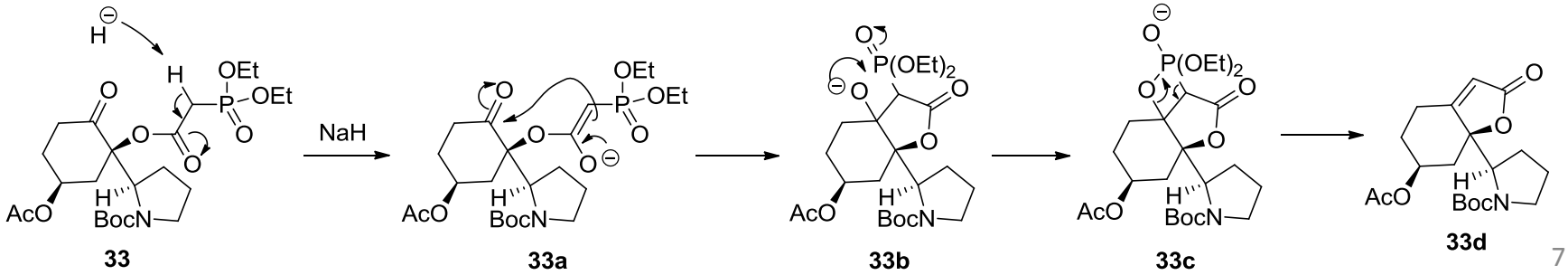
Mechanistic explanation



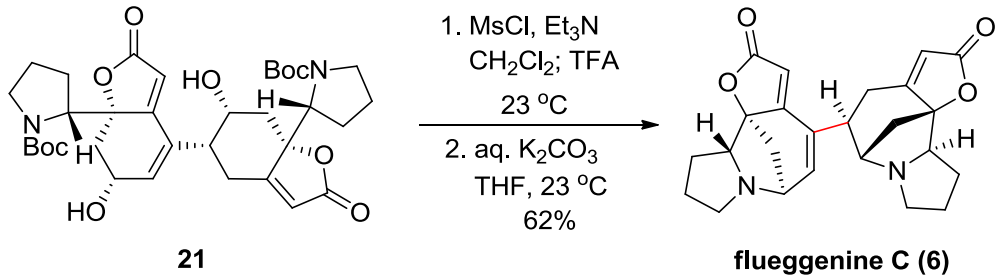
Steglich Esterification



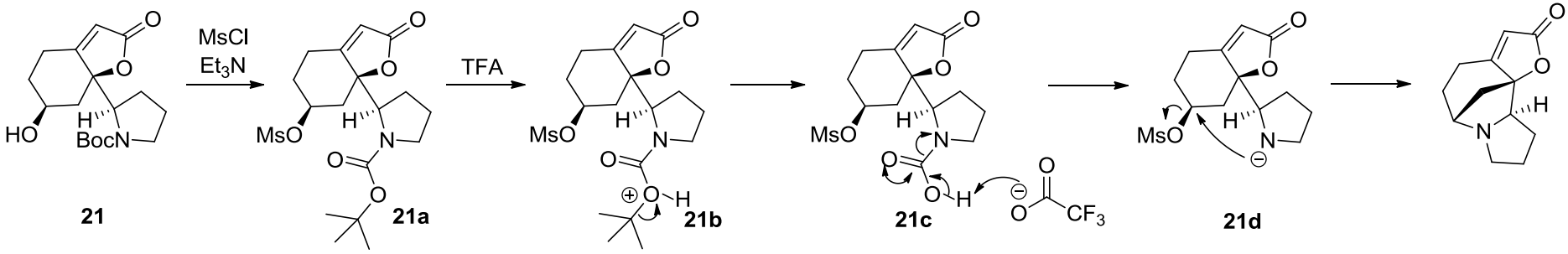
HWE reaction



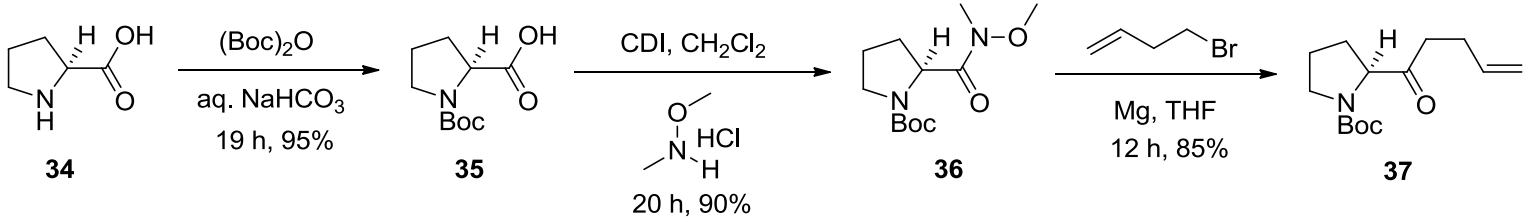
Mechanistic explanation



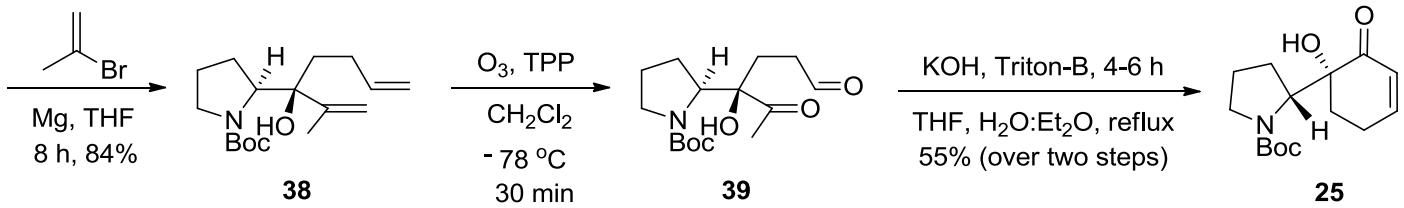
21 **flueggenine C (6)**



21 **21a** **21b** **21c** **21d**



34 **35** **36** **37**



38 **39** **25**

Mechanistic explanation