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

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D-Proline (**A**)

1-5

1) $(Boc)_2O$, $NaHCO_3$
2) CDI, MeNHOMe•HCl, DCM
3) 4-Bromo-1-butene, $BrCH_2CH_2Br$, Mg
4) Methyl propargyl ether, KO*t*-Bu; *n*-BuLi *then* product of Step 3; HCl
5) 2nd generation Grubbs catalyst

B

6-9

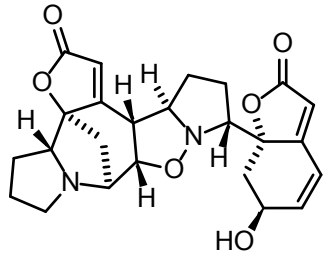
6) NBS, AIBN, CCl_4, reflux
7) TFA, *then* Et_3N
8) DCC, diethylphosphonoacetic acid
9) NaH, THF

(−)-norsecurinine (**C**)

Step 3: What is the role of $BrCH_2CH_2Br$?

Mechanism of Step 4.

Structure of Grubbs II?



(−)-flueggine A

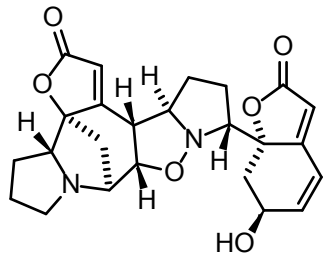
10-12

(–)-niruroidine (**D**)

13-15

E

16



(–)-flueggine A

10) TrocCl, K_2CO_3
11) $AgBF_4$, acetone, H_2O, 60 °C
12) Zn, AcOH, H_2O
then $NH_3 \cdot H_2O$

13) Dess-Martin periodinane
14) $NaBH_4$, MeOH
15) Na_2WO_4, H_2O_2

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

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

Treatment of **D** with PPh_3 and DIAD triggers 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-dipol do you know?

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