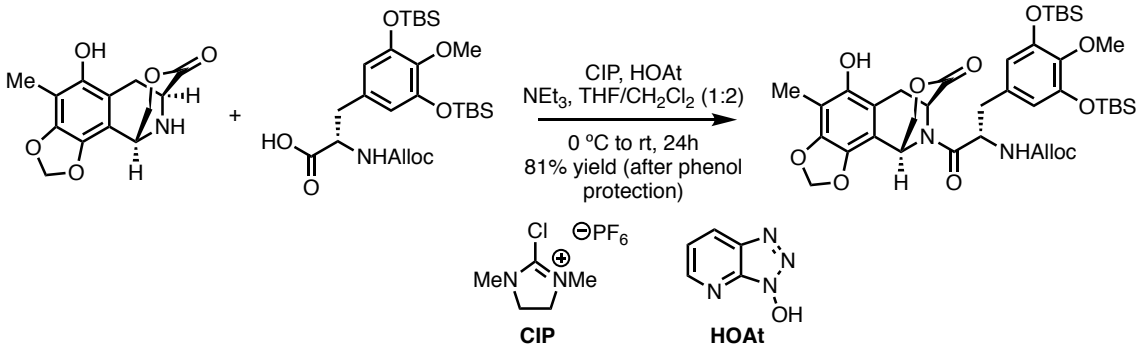
**Problem Set (Nelli)**

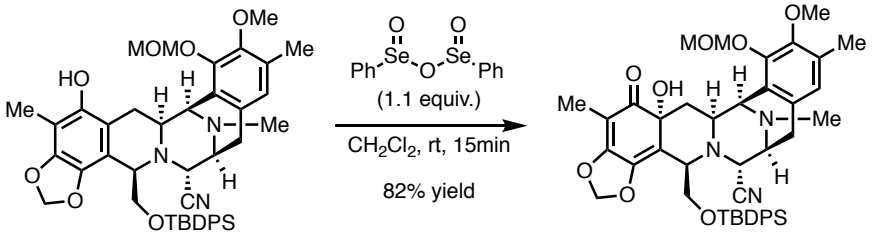
**(1)** In Corey's formal synthesis of ecteinascidin 743 from 2000, a peptide coupling with a chloro-imidazolidinium reagent and hydroxy-azabenzotriazole reagent are used to unite two key fragments. Ref: Martinez, E.J.; Corey, E.J., *Org. Lett.* **2000**, *2*, 993-996.

Draw the mechanism for this peptide coupling. What is the purpose of the hydroxy-azabenzotriazole (HOAt)? Would this reaction work without HOAt?



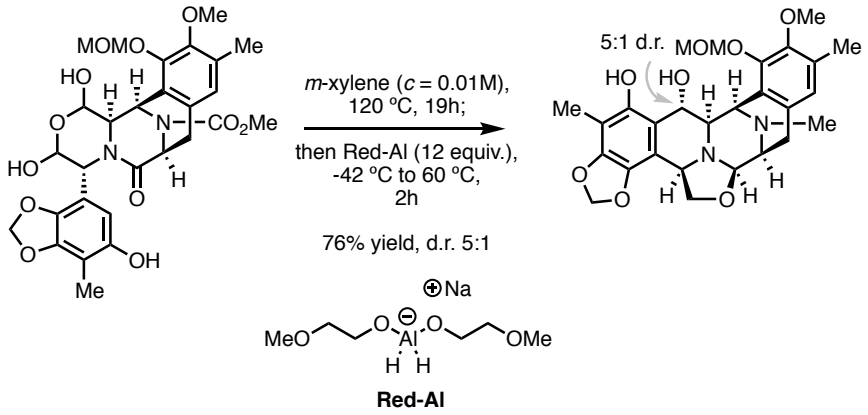

**(2)** Enroute to the cyclic sulfide of ecteinascidin 743, Corey and coworkers aimed to oxidize the phenol of the tetrahydroisoquinoline. This was accomplished via a procedure developed by Barton in 1976 (ref: Barton, D.H.R.; *et al., J. Chem. Soc., Chem. Commun.* **1976**, 985-986.) using diphenylseleninic anhydride. Ref: Corey, E.J.; Gin, D.Y.; Kania, R.S., *J. Am. Chem. Soc.* **1996**, *118*, 9202-9203.

How does this oxidation take place? Draw a mechanism.



**(3)** In their second-generation synthesis of ecteinascidin 743, Fukuyama and coworkers complete the pentacyclic core of the natural product from the bis-hemiacetal shown below. Ref: Kawagishi, F.; Toma, T.; Inui, T.; Yokoshima, S.; Fukyuama, T., *J. Am. Chem. Soc.* **2013**, *135*, 13684-13687.

Draw a mechanism for this reaction.




**Red-Al**