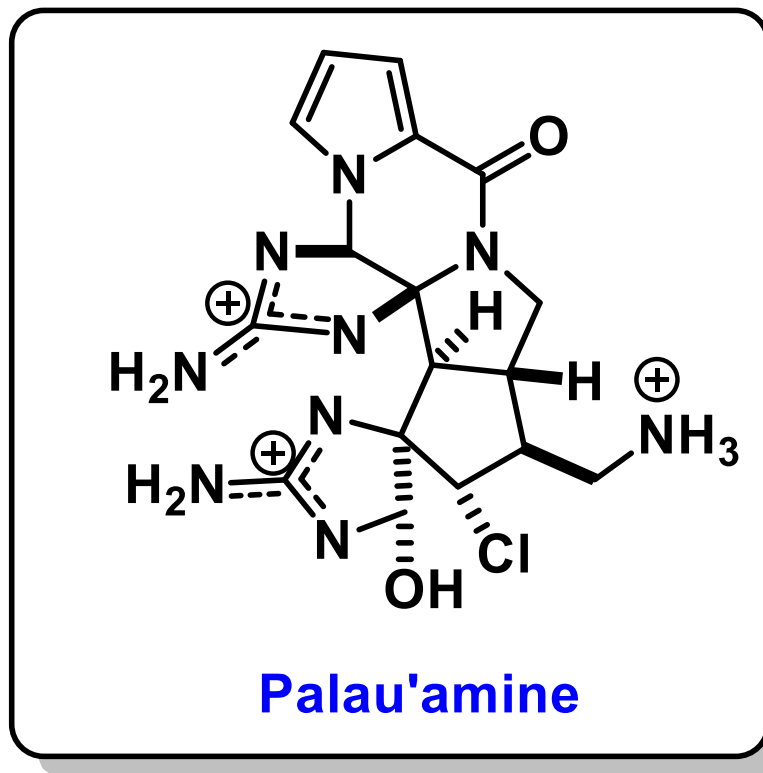
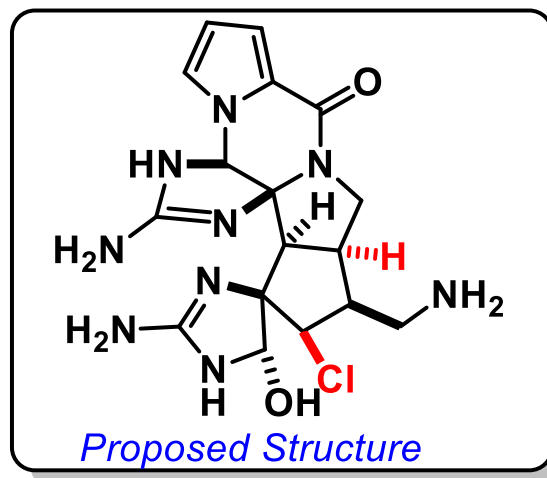
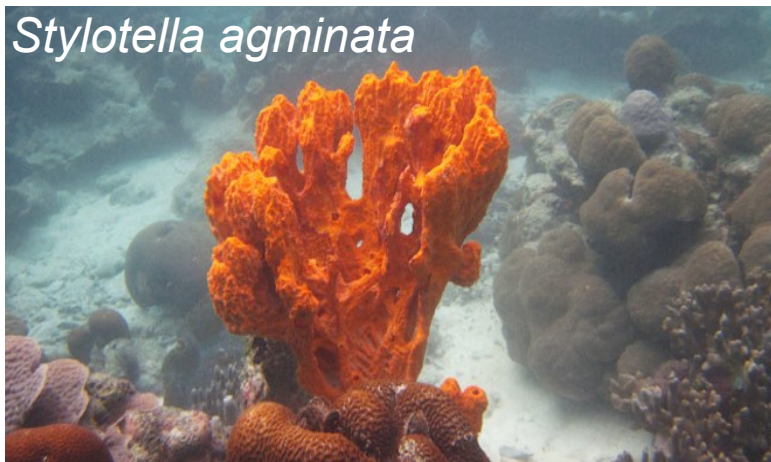


Total Synthesis of (-)-Palau'amine



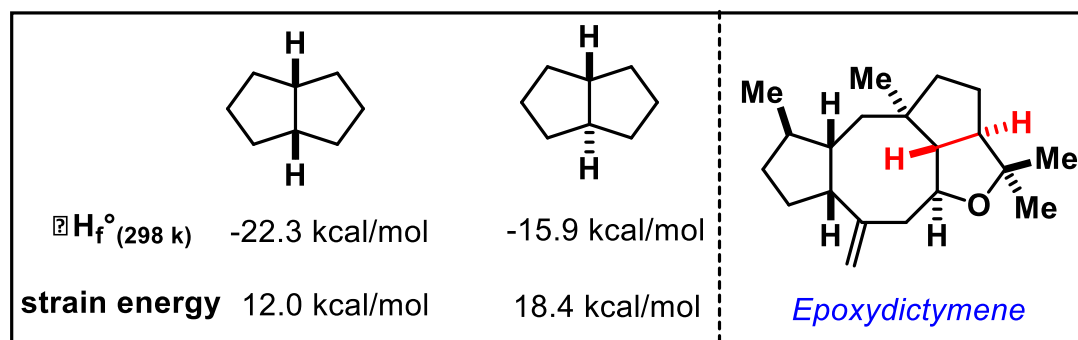
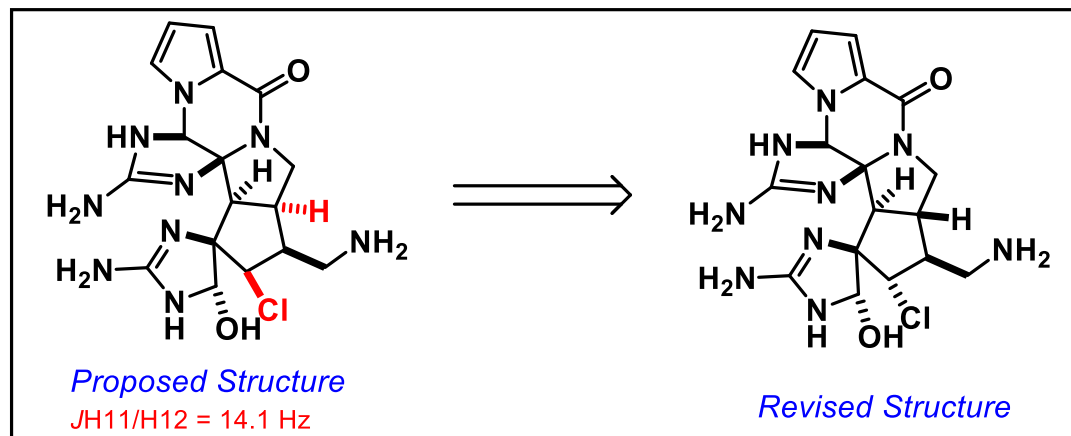
Srinivas R Paladugu
Looper Group
03/27/2018

Isolation



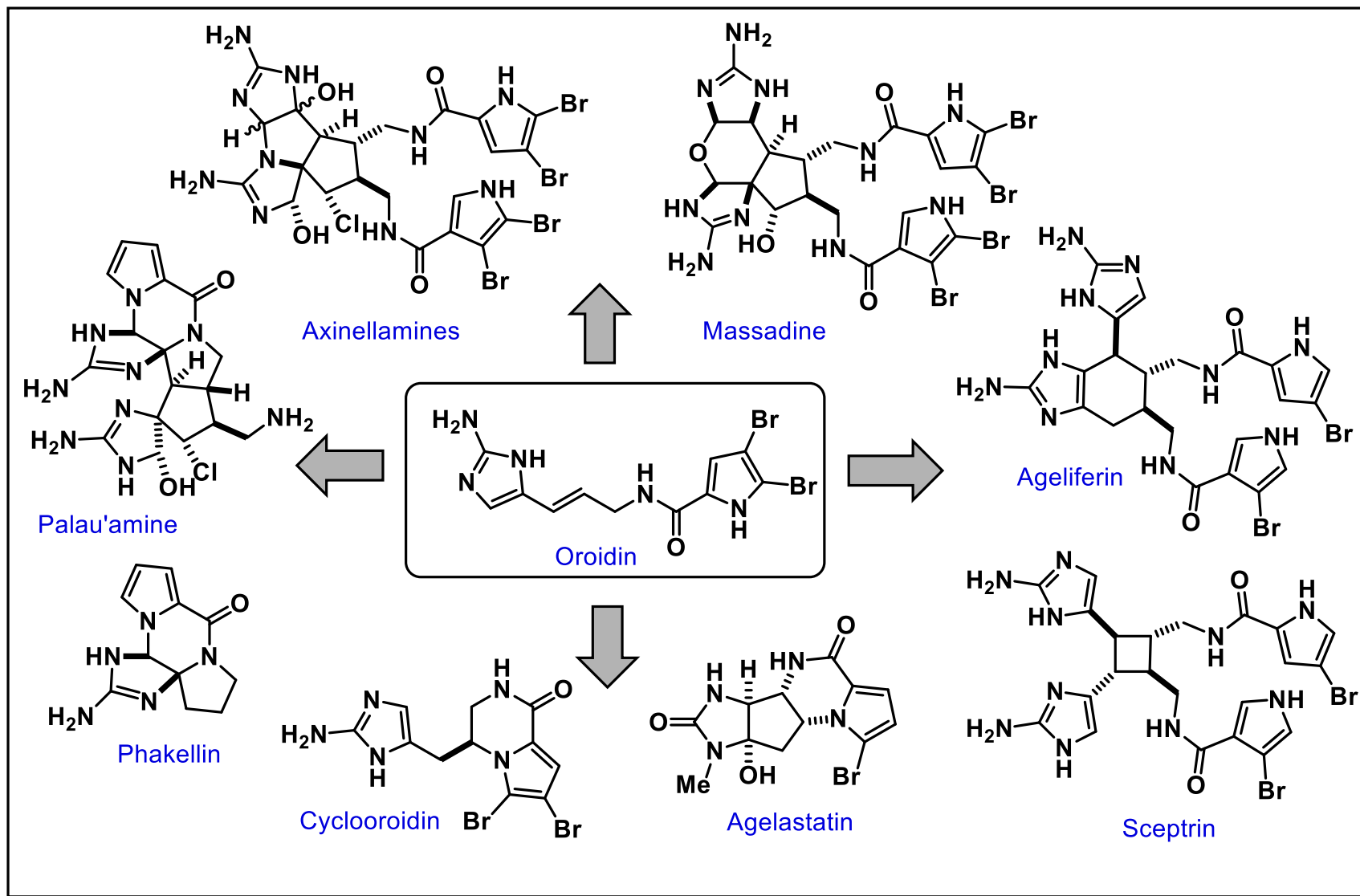
- ❖ Isolated from the sea sponge *Stylotella agminate* in 1993 by Scheuer and colleagues
- ❖ Belongs to a family of Pyrrole-Imidazole alkaloid family
- ❖ Shows wide range of biological properties including antifungal, antitumor and immunosuppressive activities

Revised Structure

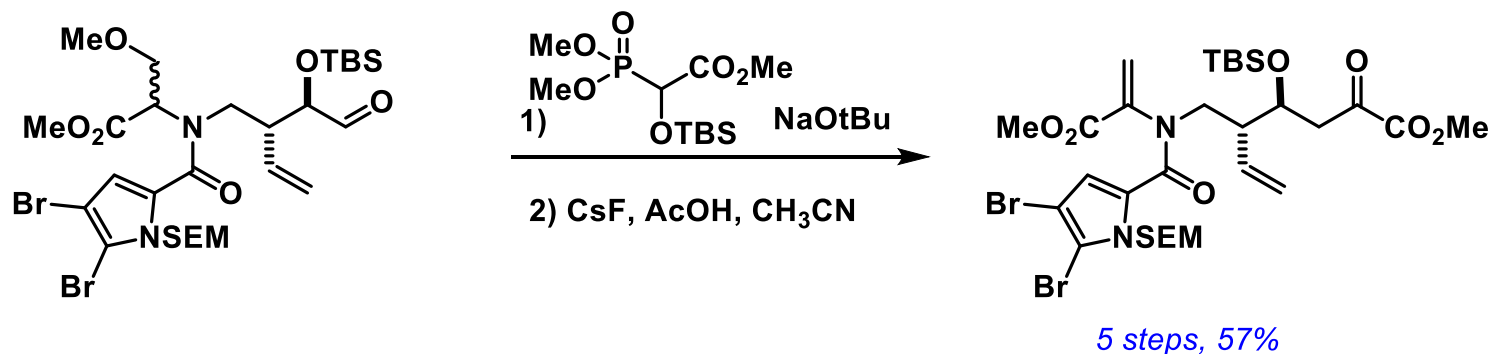
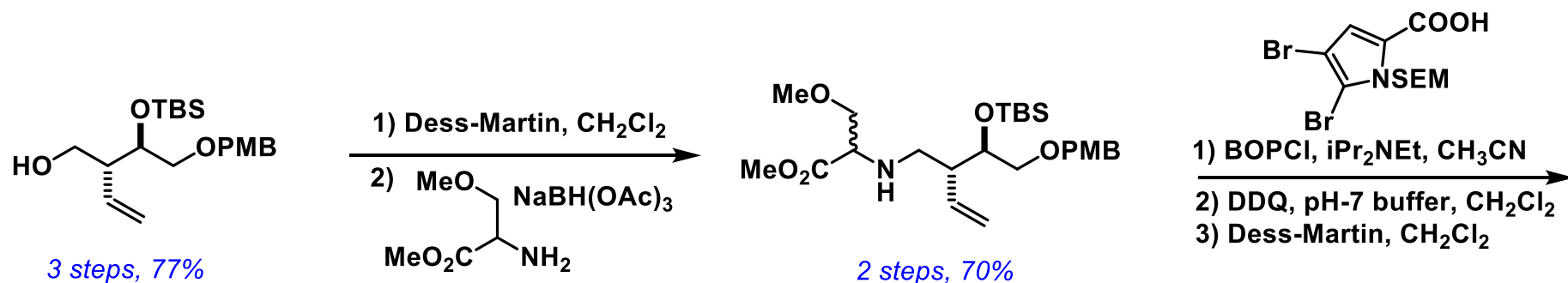
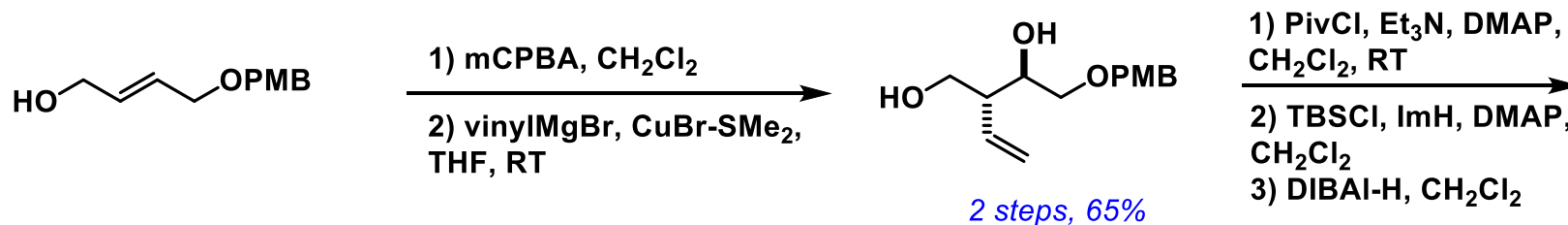


- ❖ Fully substituted cyclopentane ring with eight stereogenic centers and a trans bicyclo [3.3.0] octane
- ❖ Noncrystalline, redox labile, pH sensitive alkaloid, high nitrogen content (N/C ~ 1/2)
- ❖ Daunting challenge
 ~40 Synthetic approaches
 ~30 PhD dissertations
 2 total synthesis

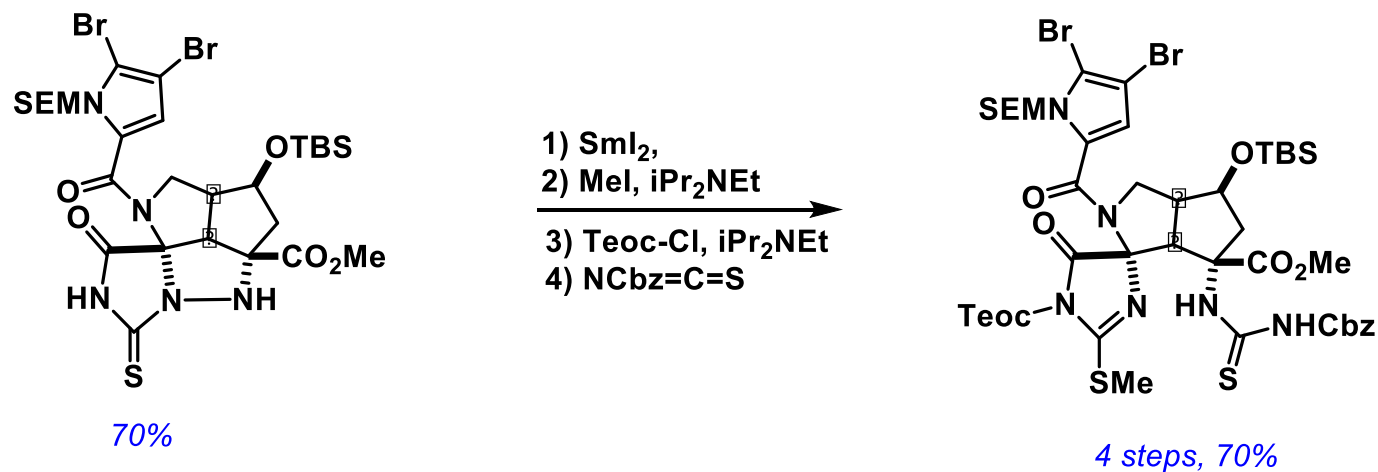
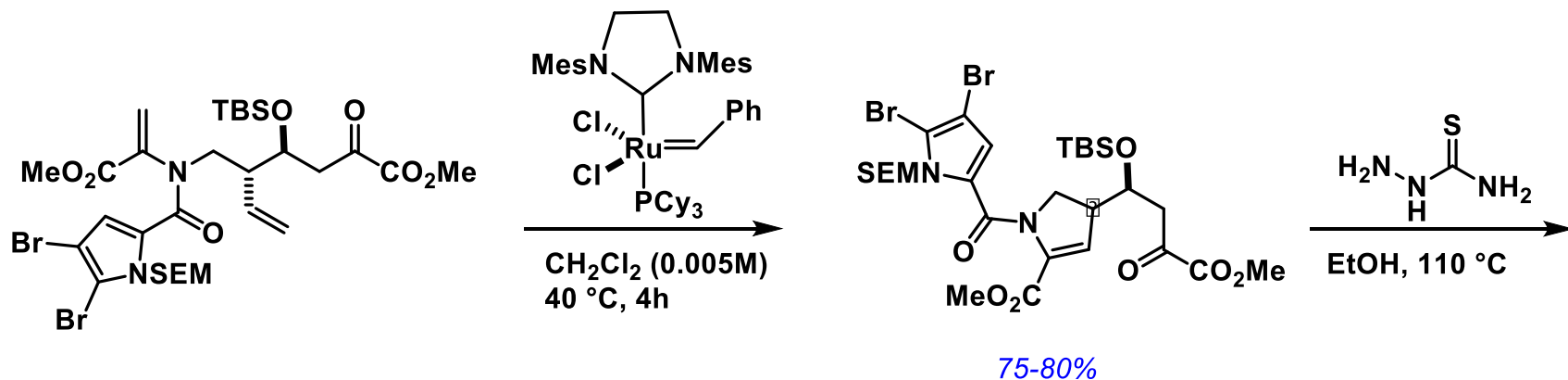
Pyrrole-Imidazole Alkaloids



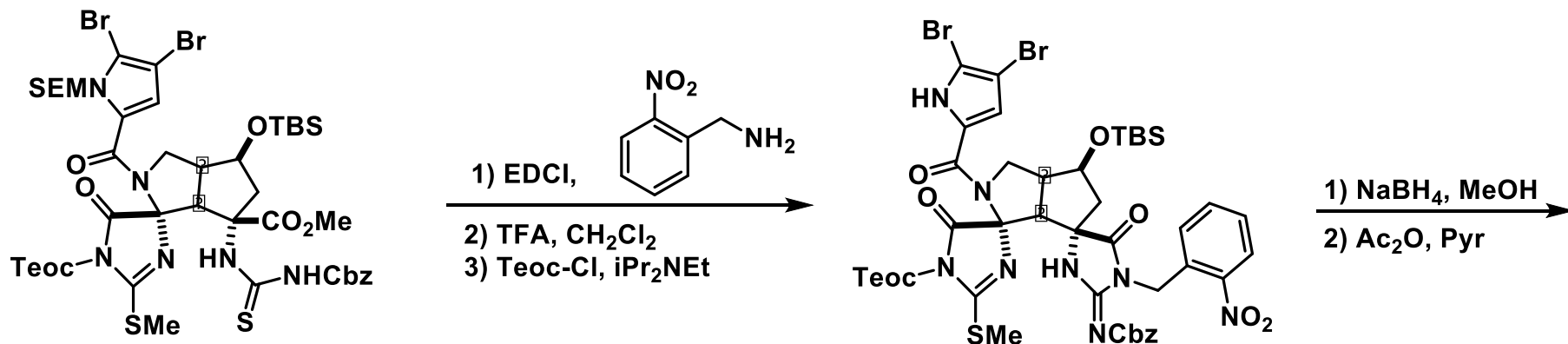
Overman Synthesis Toward Palau'amine



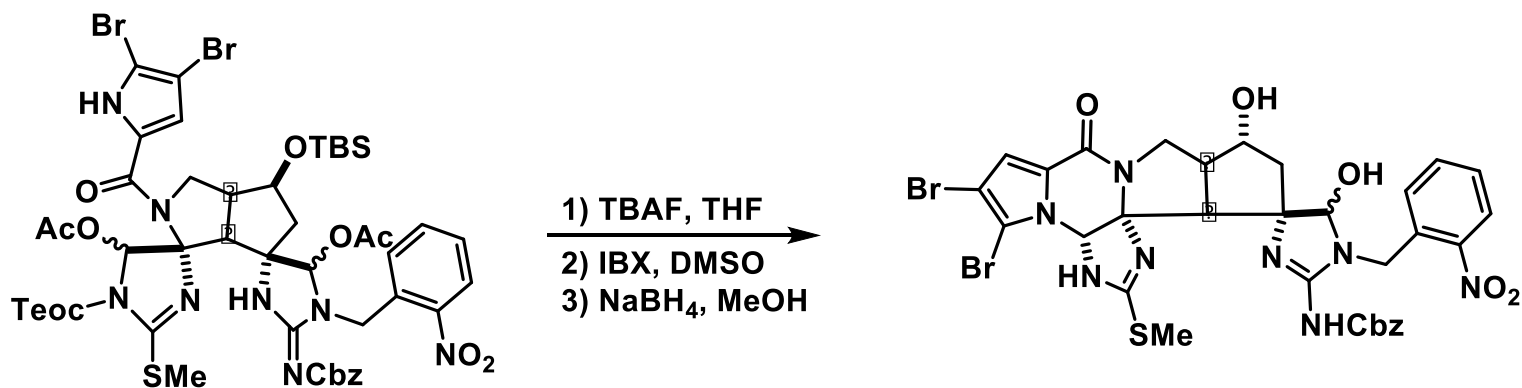
Overman Synthesis Toward Palau'amine



Overman Synthesis Toward Palau'amine



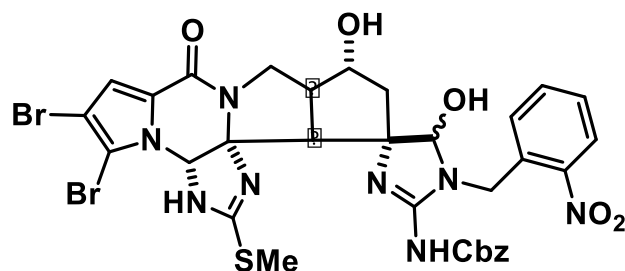
3 steps, 78%



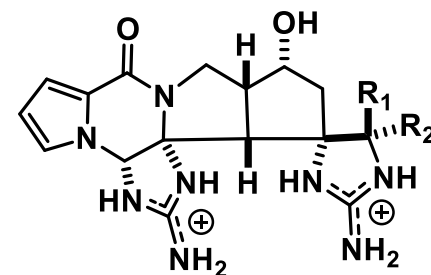
2 steps, 60%

3 steps, 86%

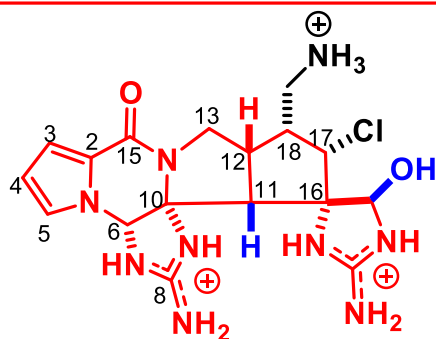
Overman Synthesis Toward Palau'amine



- 1) mCPBA, CH₂Cl₂
- 2) NH₃, CH₂Cl₂
- 3) hv, dioxane
- 4) H₂, Pd/C, 0.1%TFA



$R_1 = OH, R_2 = H, 43\%$
 $R_1 = H, R_2 = OH, 22\%$

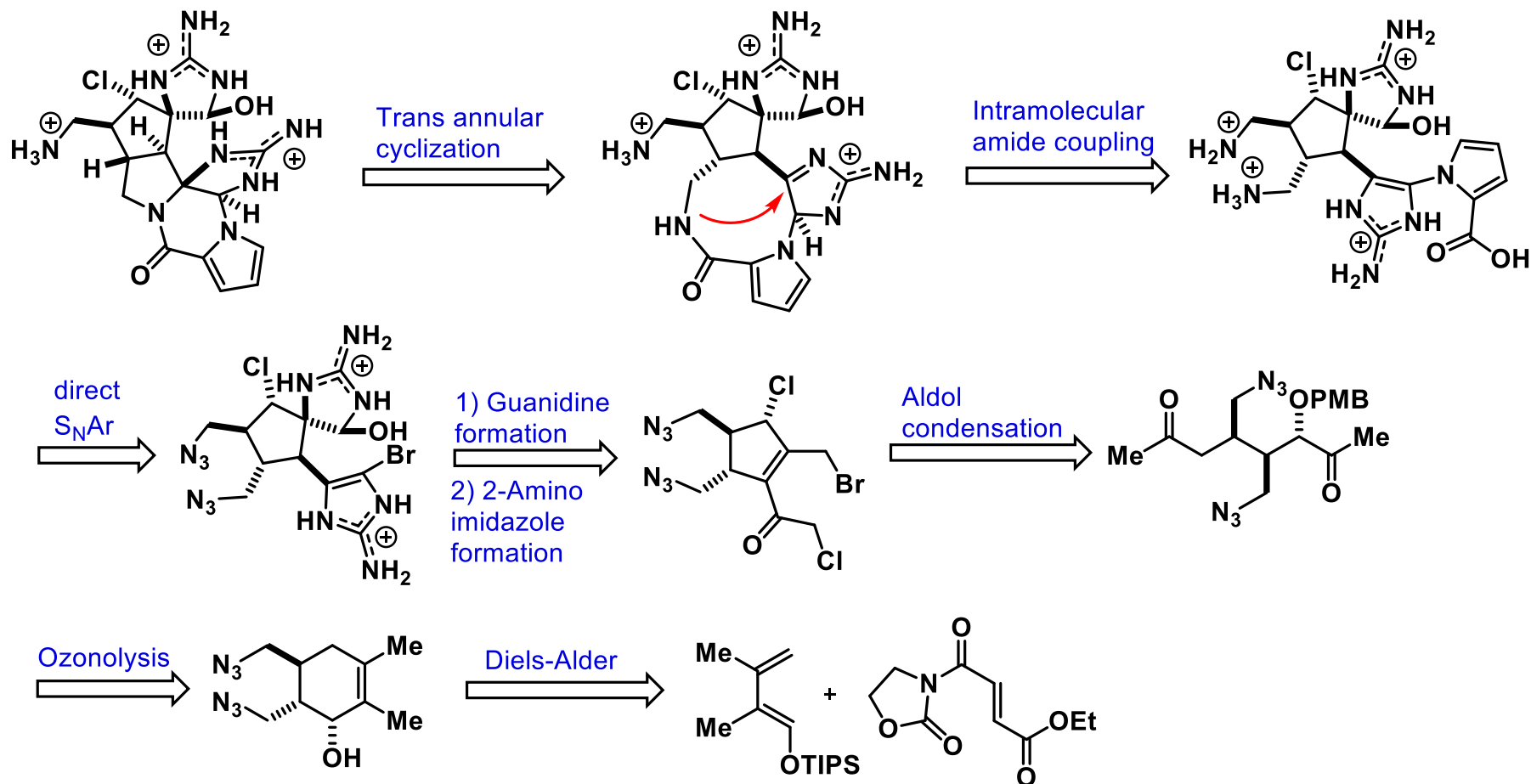


Palau'amine
Original Structure

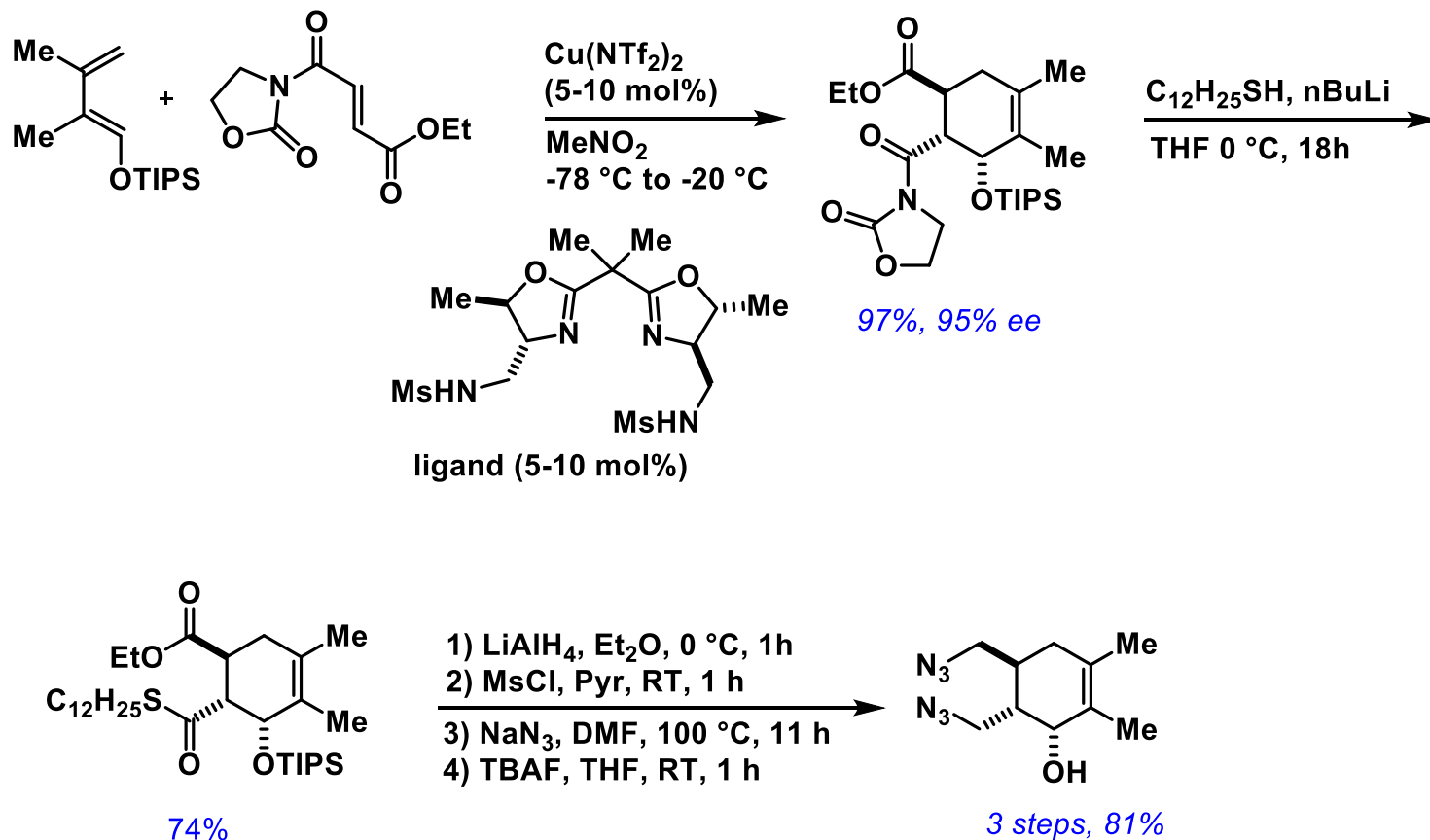
Table 1. ¹H and ¹³C NMR Data for Palau'amine,^{2b} 3, and 4 in D₂O

carbon	palau'amine		3		4	
	¹³ C, ppm	¹ H, ppm (mult, J [Hz])	¹³ C, ppm	¹ H, ppm (mult, J [Hz])	¹³ C, ppm	¹ H, ppm (mult, J [Hz])
2	122.5		120.5		120.3	
3	115.6	6.85, (dd, J = 3.9, 1.5)	115.0	6.97, (dd, J = 4.0, 1.3)	115.0	6.97, (dd, J = 4.0, 1.3)
4	113.8	6.35, (dd, J = 3.9, 2.8)	113.0	6.47, (dd, J = 4.0, 2.7)	113.2	6.47, (dd, J = 4.0, 2.7)
5	125.2	6.99, (dd, J = 2.8, 1.5)	124.7	7.13, (dd, J = 2.7, 1.3)	124.5	7.10, (dd, J = 2.7, 1.3)
6	69.0	6.33, (s)	68.1	6.36, (s)	68.7	6.24, (s)
8	157.8		156.9		156.7	
10	80.8		82.0		81.8	
11	56.3	3.08, (d, J = 14.1)	53.1	3.82, (d, J = 12.0)	59.9	3.35, (d, J = 10.7)
12	41.8	2.52, (dddd)	45.3	3.07, (dddd, J = 12.0, 10.1, 6.1, 4.1)	44.2	3.15, (dddd, J = 10.7, 9.9, 5.1, 4.6)
13	46.1	3.96, (dd, J = 10.4, 7.3)	42.2	4.16, (β) (dd, J = 12.3, 10.1)	42.7	4.07, (β) (dd, J = 12.3, 9.9)
		3.28, (dd, J = 10.3, 10.4)		3.65, (α) (dd, J = 12.3, 6.1)		3.72, (α) (dd, J = 12.3, 4.6)
15	159.5		157.4		157.4	
16	72.1		71.9		70.7	
17	74.0	4.35, (d, J = 7.9)	49.9	2.35, (β) (dd, J = 14.3, 3.7)	41.2	2.79, (β) (dd, J = 15.4, 5.1)
				2.16, (α) (d, J = 14.3)		2.02, (α) (dd, J = 15.4, 2.5)
18	48.6	2.47, (dddd)	70.1	4.34, (m)	69.2	4.34, (m)
19	41.9	3.32, (dd, J = 13.2, 7.0)				
		3.24, (dd, J = 13.2, 7.0)				
20	83.7	5.96, (s)	85.8	5.34, (s)	87.9	5.19, (s)
22	157.9		158.7		158.7	

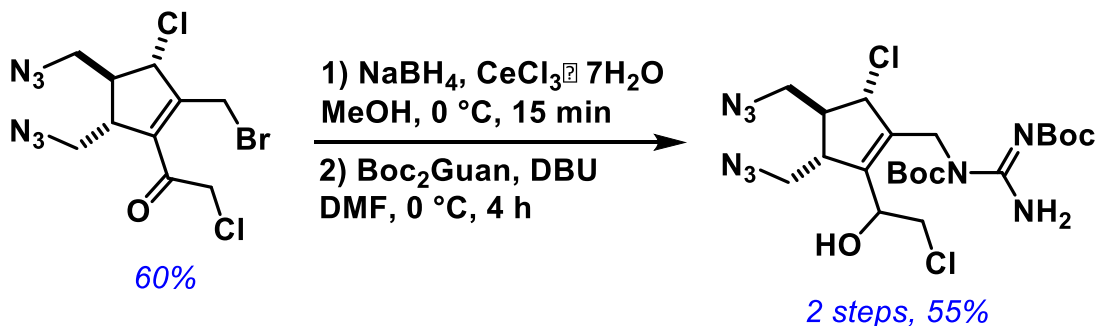
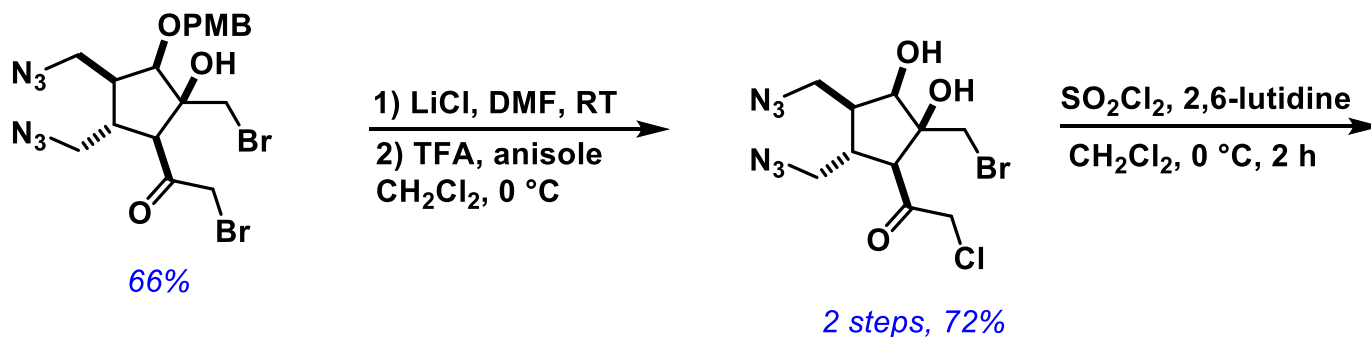
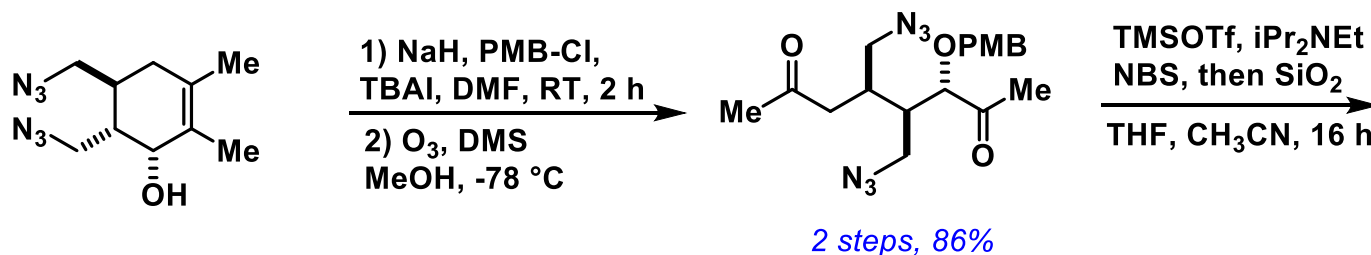
Baran Synthesis of Palau'amine



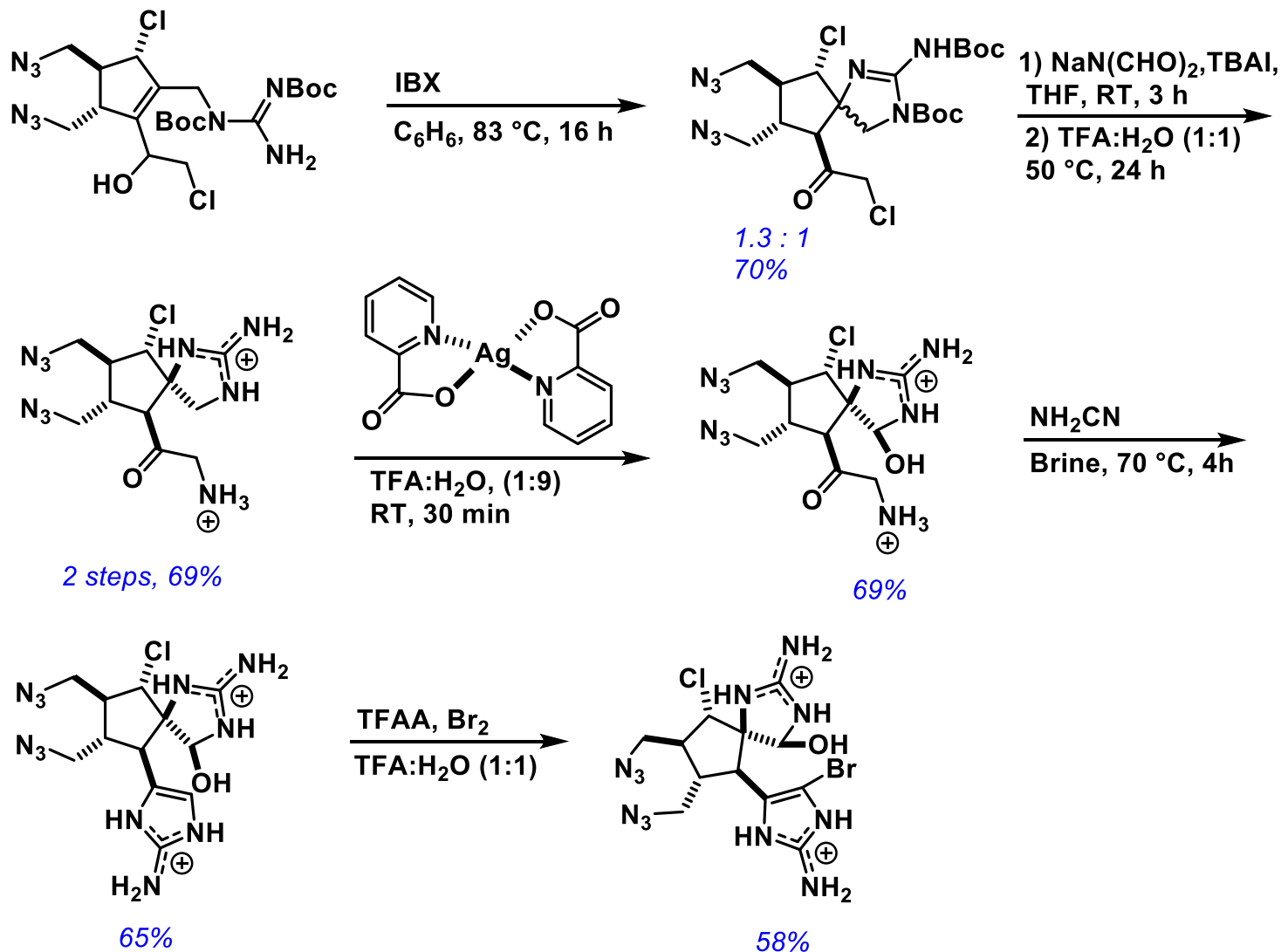
Baran Synthesis of Palau'amine



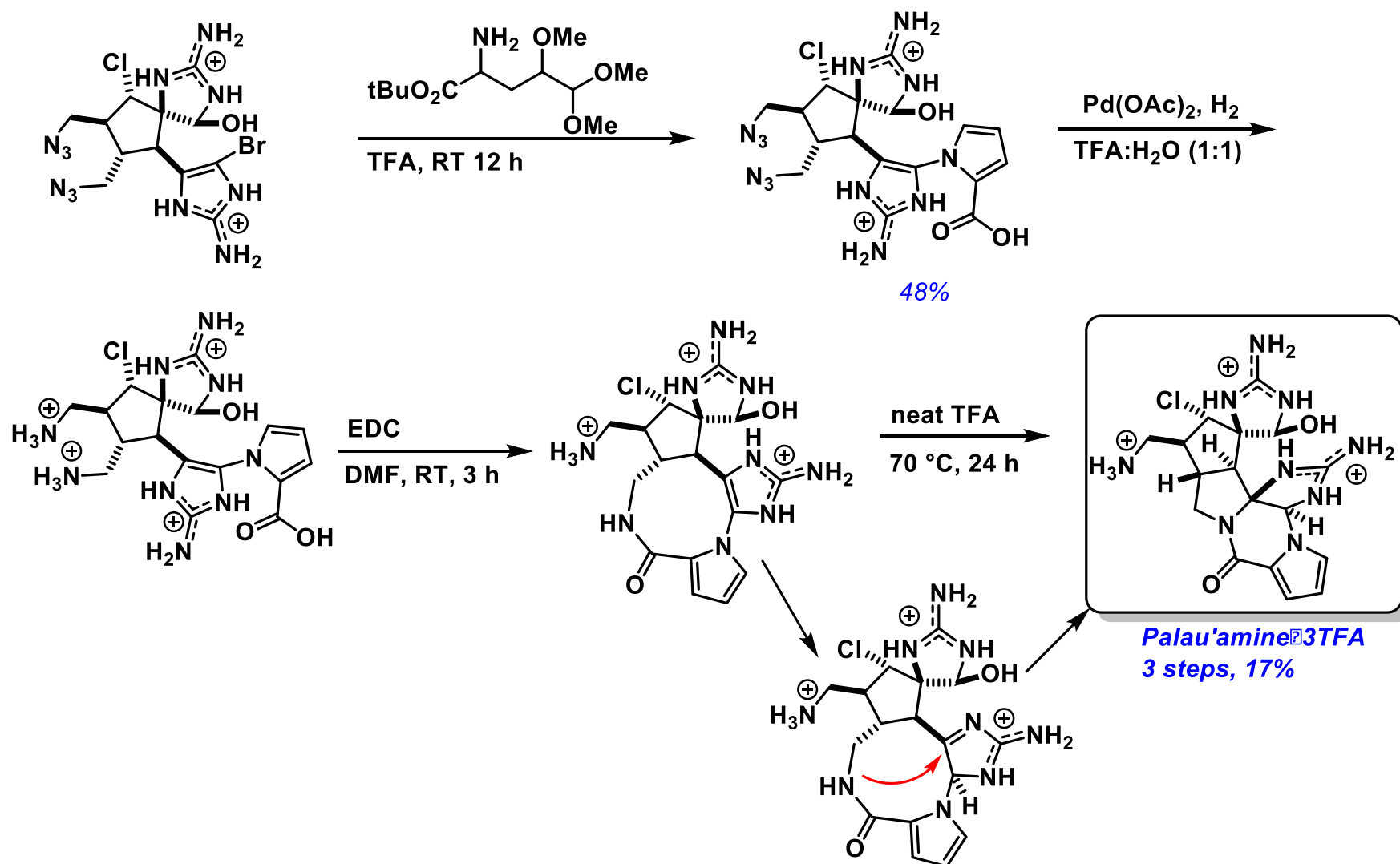
Baran Synthesis of Palau'amine



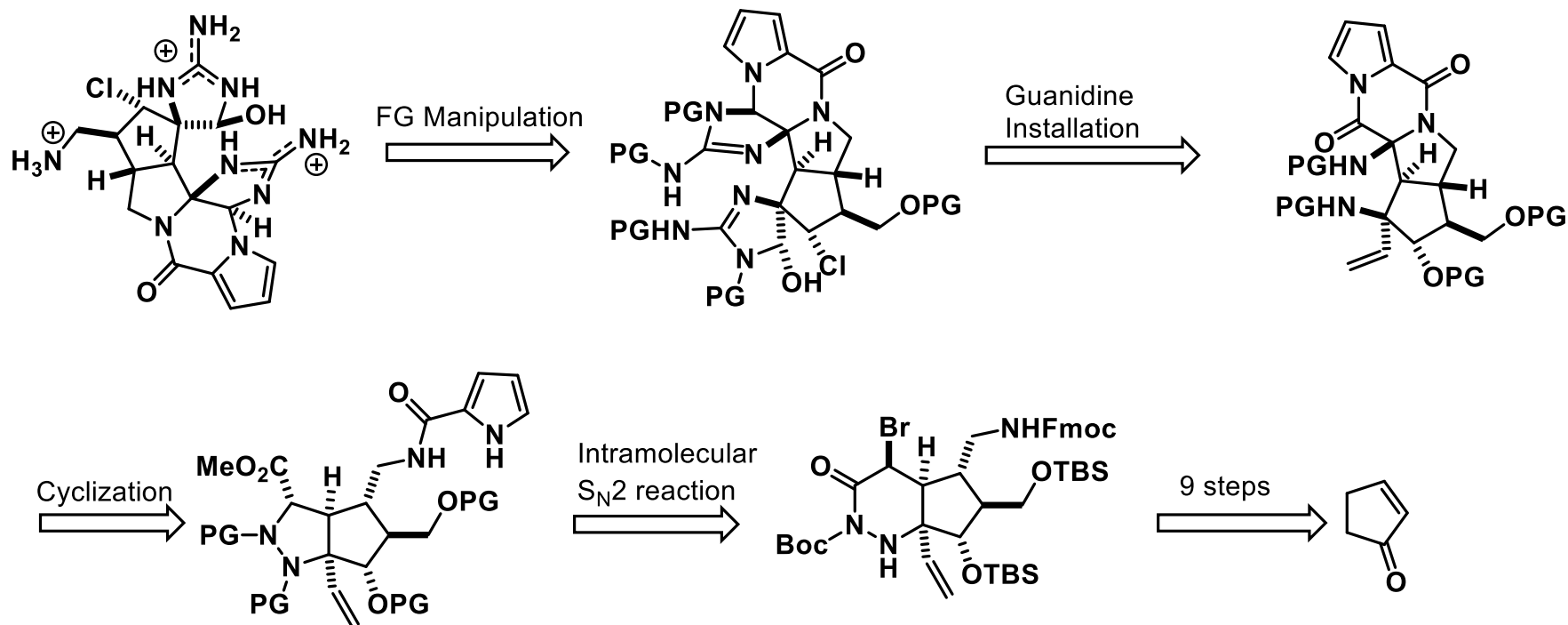
Baran Synthesis of Palau'amine



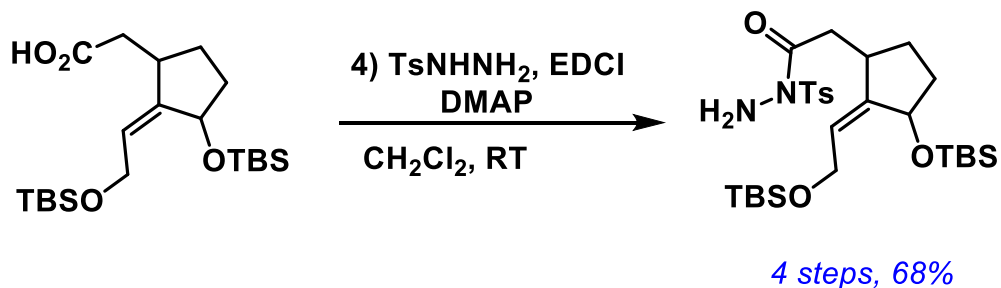
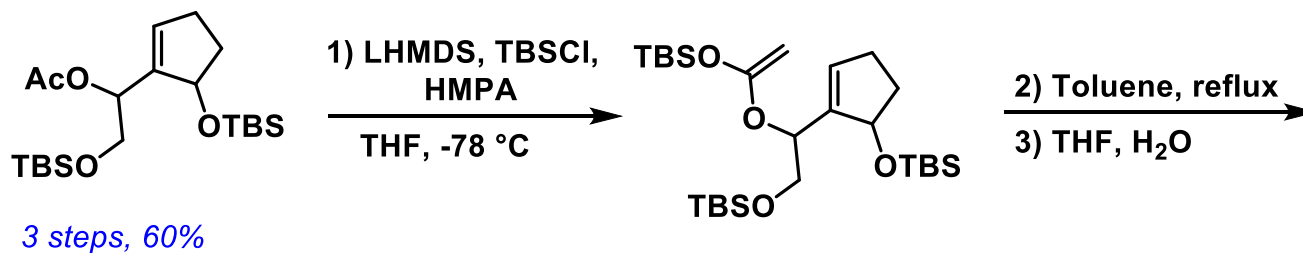
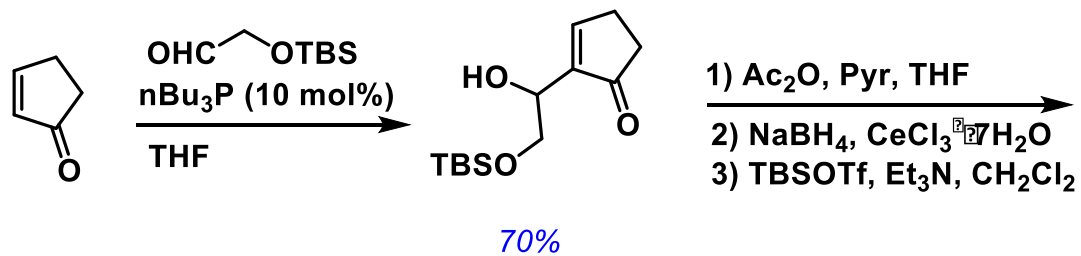
Baran Synthesis of Palau'amine



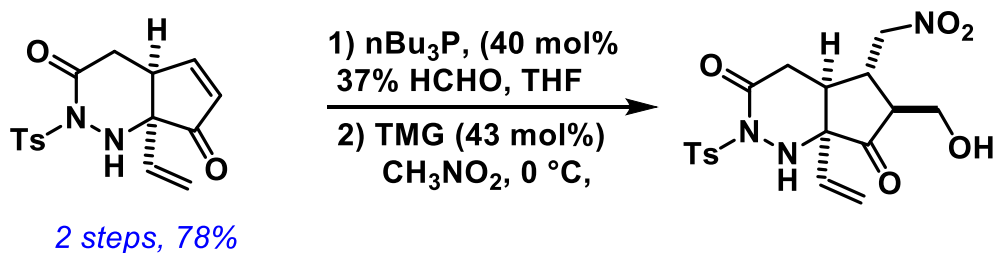
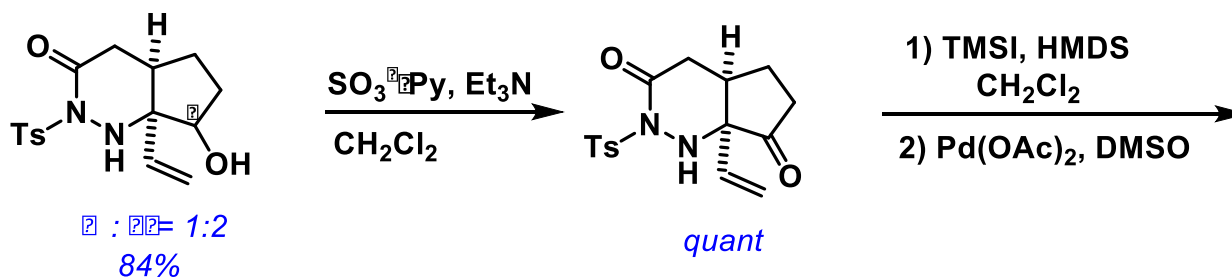
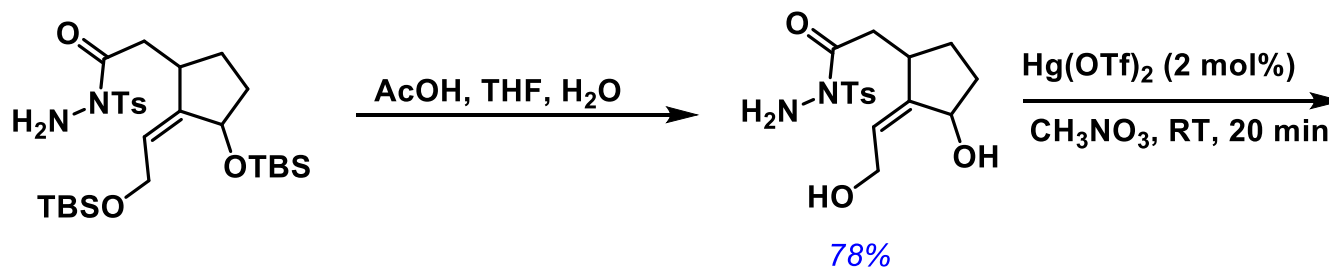
Namba Synthesis of Palau'amine



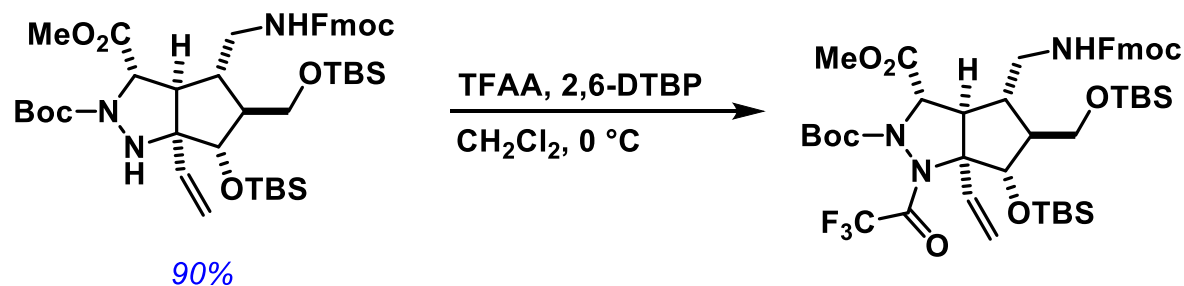
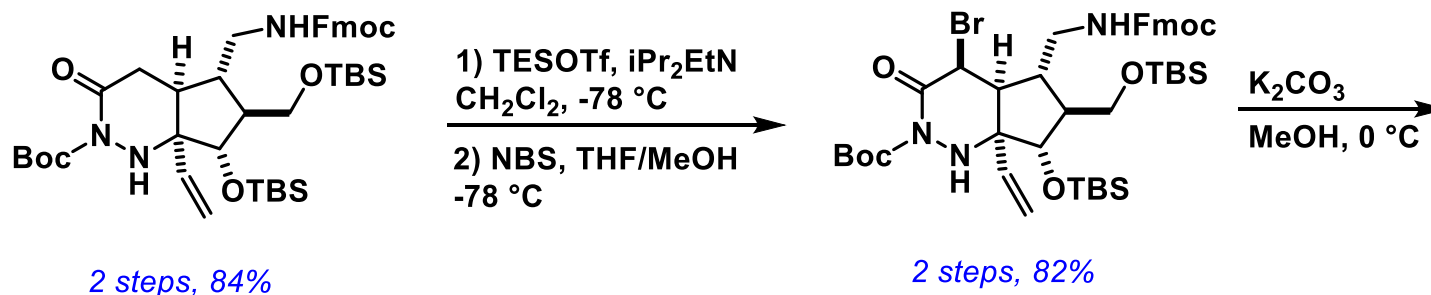
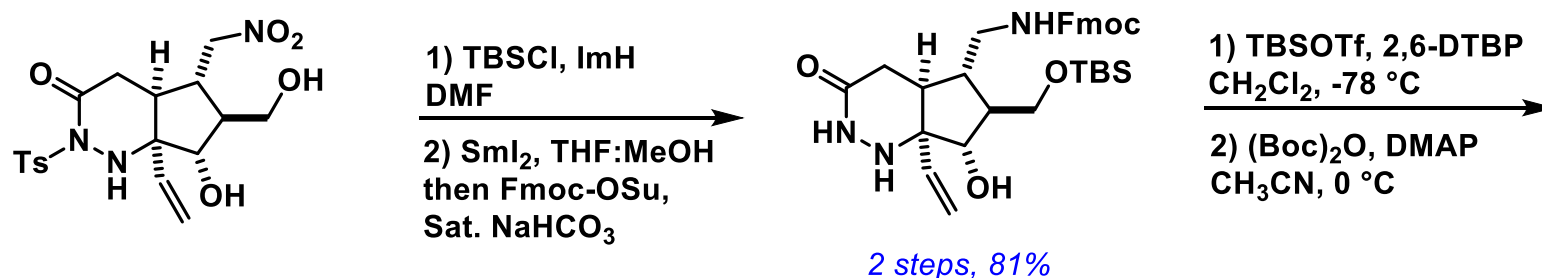
Namba Synthesis of Palau'amine



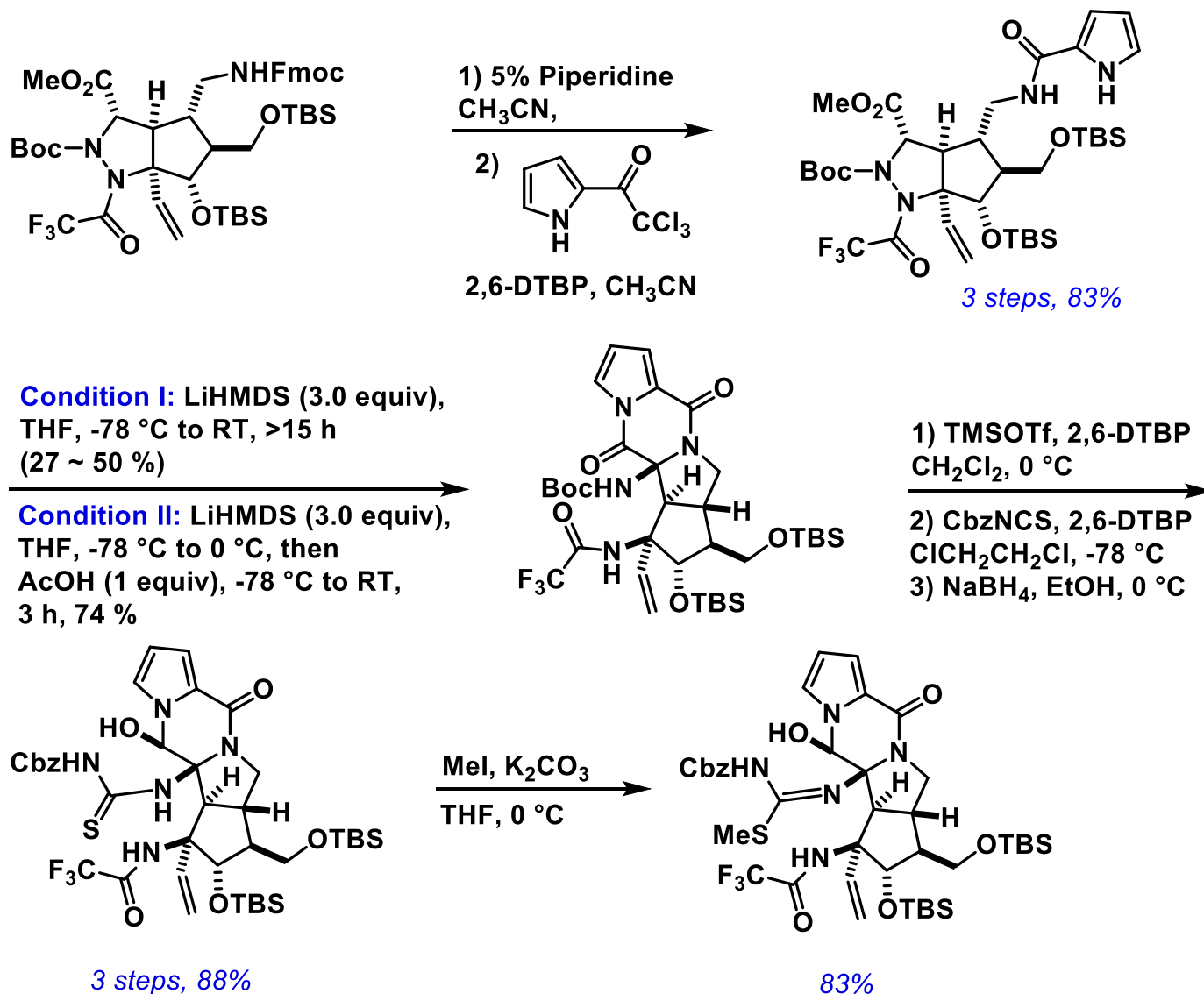
Namba Synthesis of Palau'amine



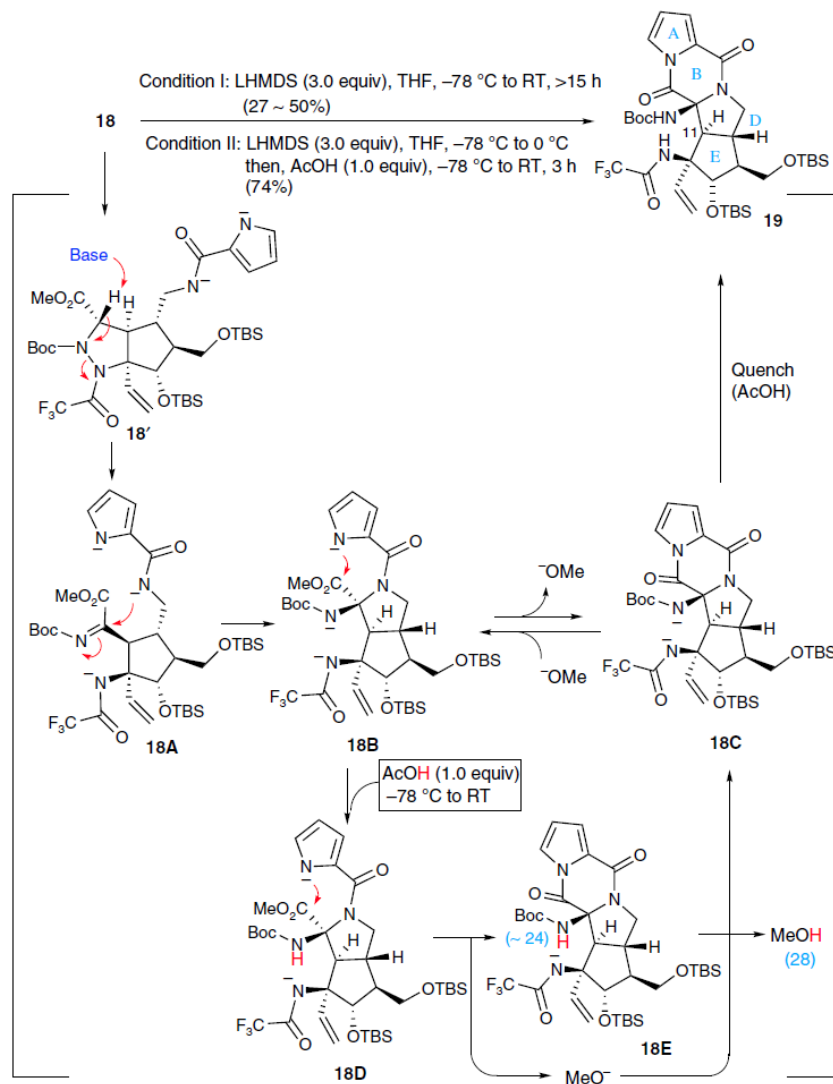
Namba Synthesis of Palau'amine



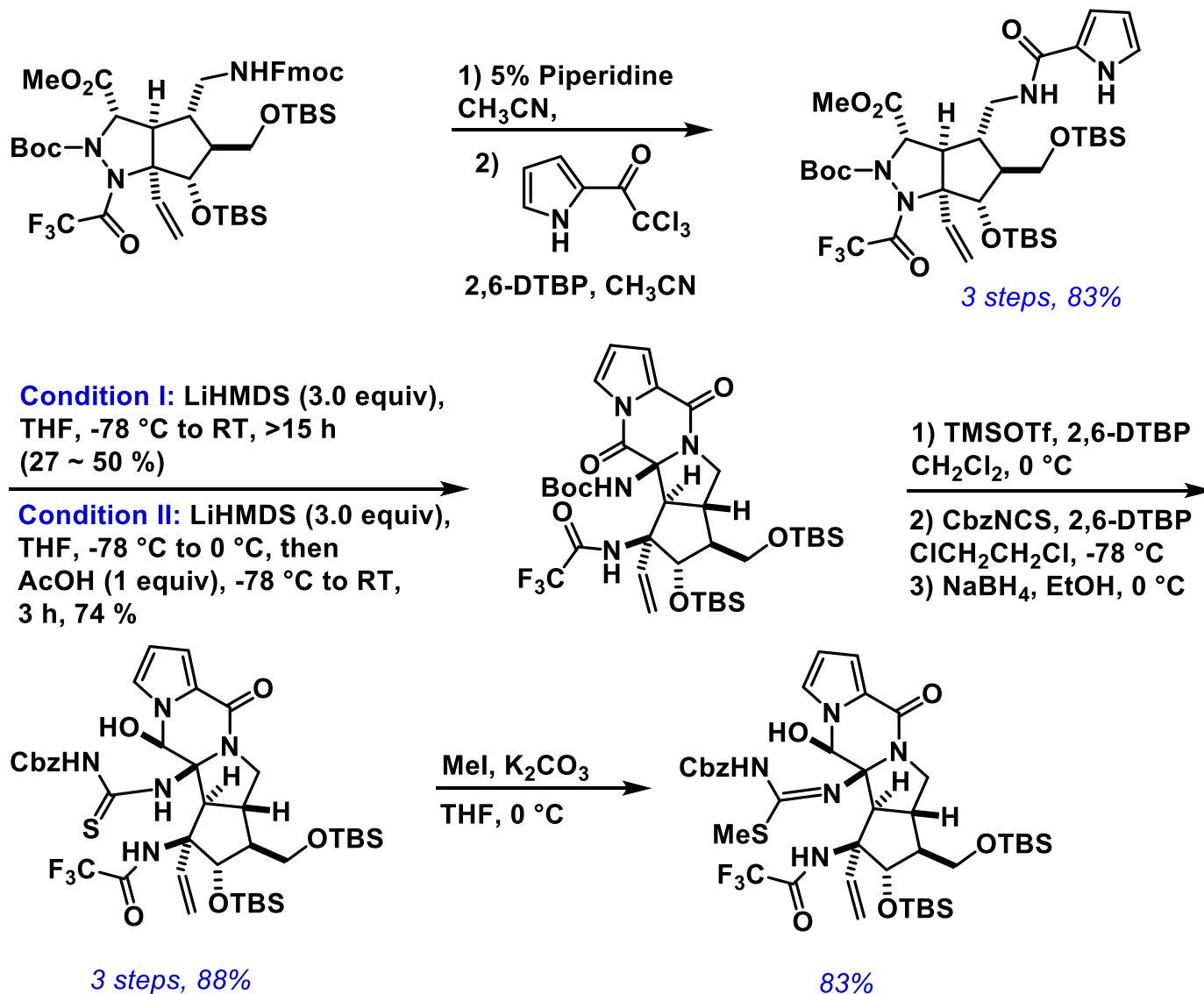
Namba Synthesis of Palau'amine



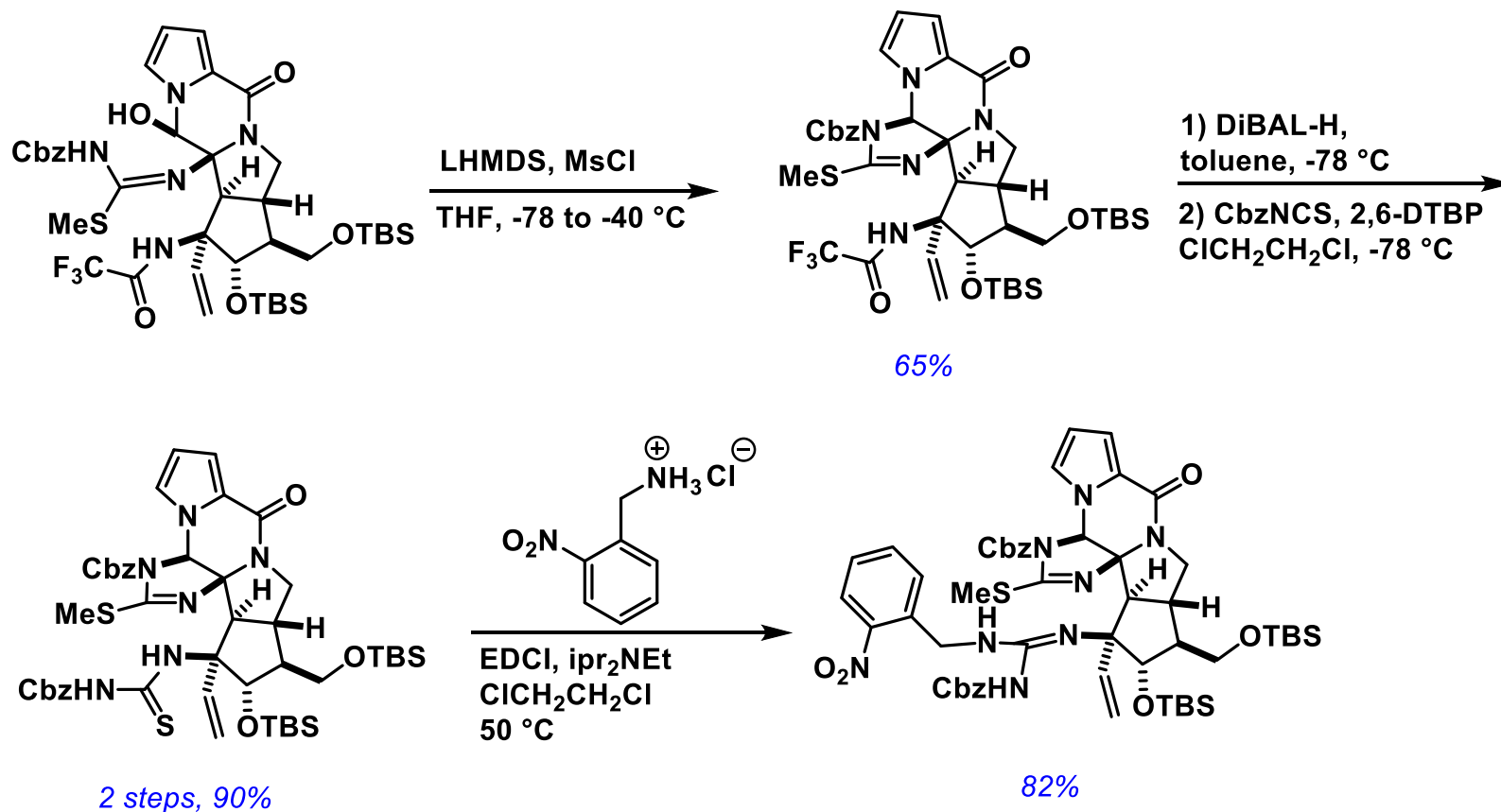
Namba Synthesis of Palau'amine



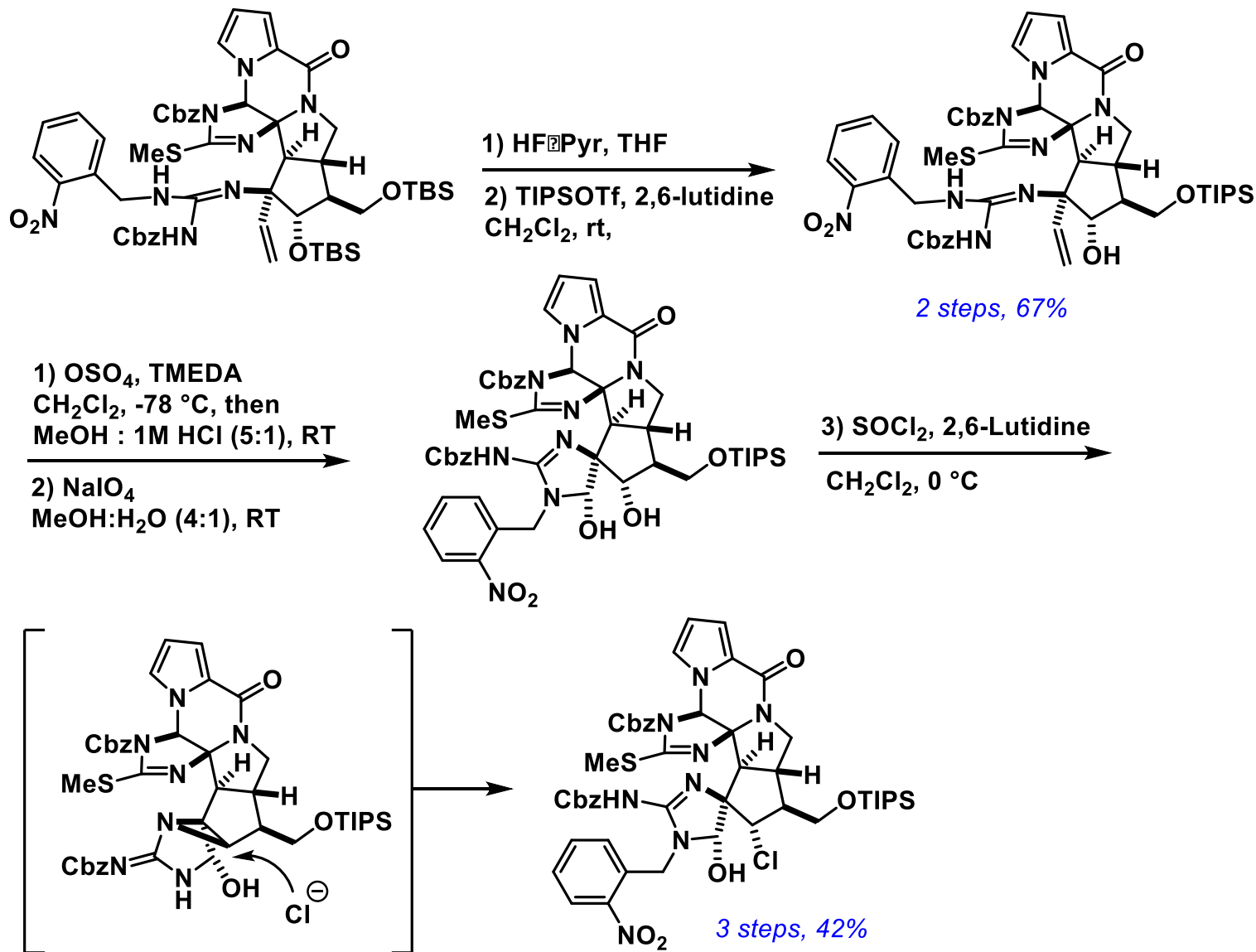
Namba Synthesis of Palau'amine



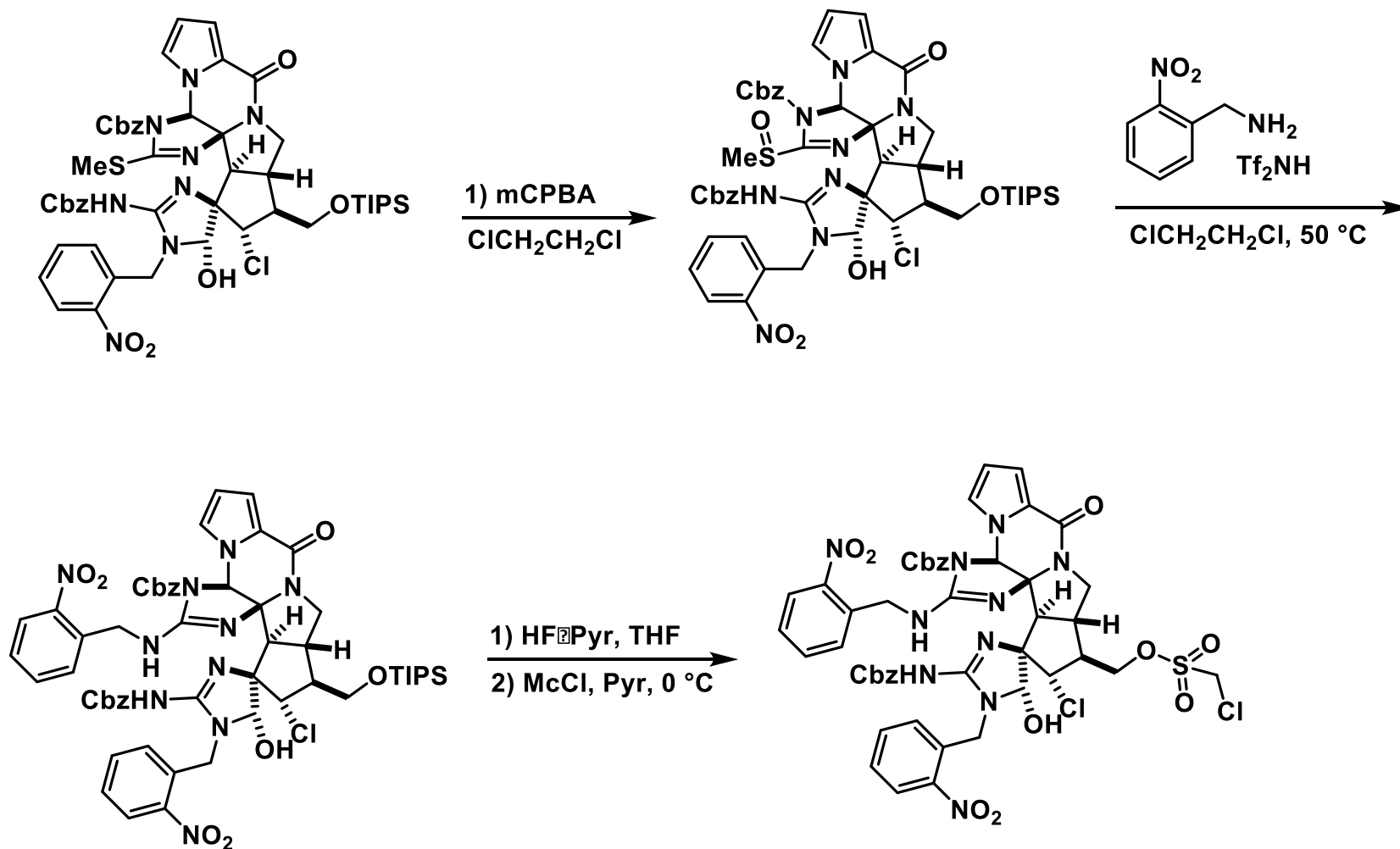
Namba Synthesis of Palau'amine



Namba Synthesis of Palau'amine

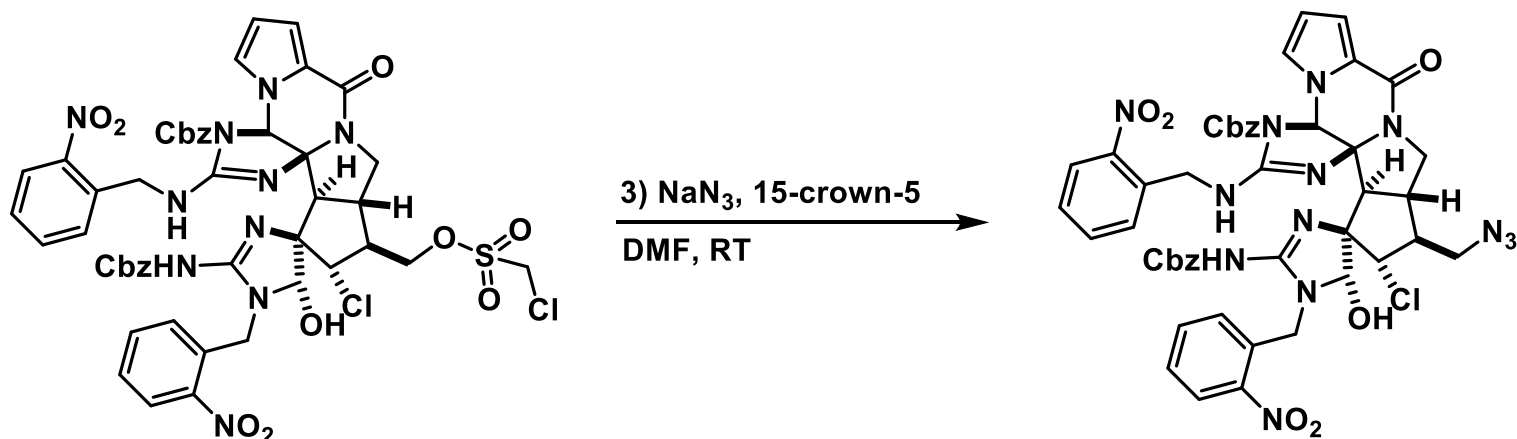


Namba Synthesis of Palau'amine

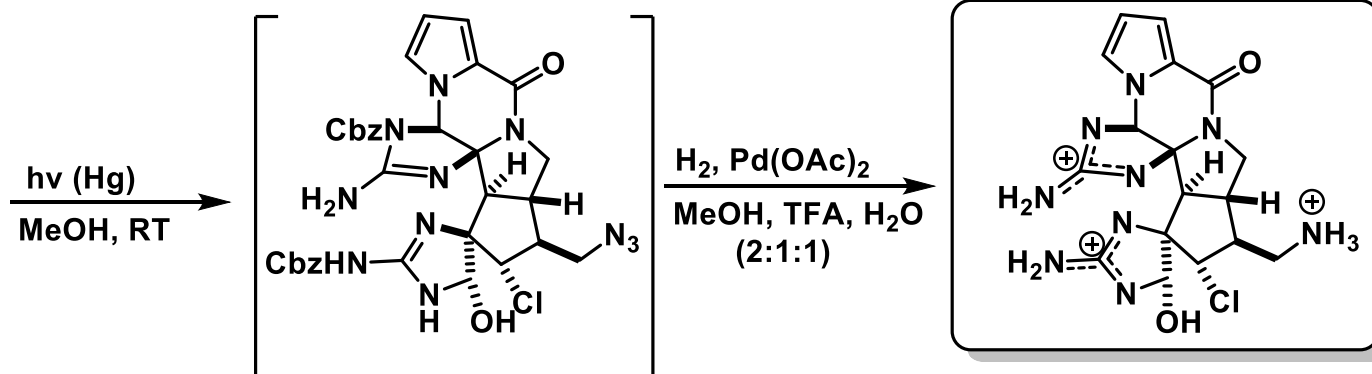


2 steps, 70%

Namba Synthesis of Palau'amine

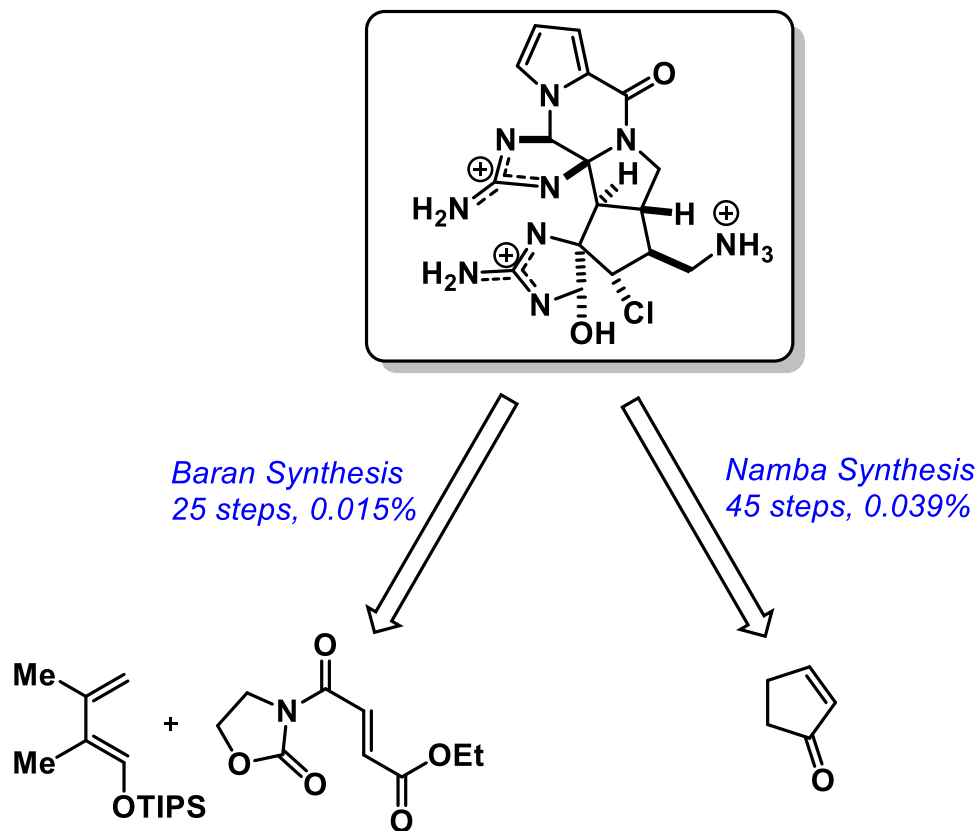


3 steps, 45%



Palau'amine·3TFA
2 steps, 64%

Summary



Seiple, I. B.; Su, S.; Young, I. S.; Nakamura, A.; Yamaguchi, J.; Jørgensen, L.; Rodriguez, R. A.; O'Malley, D. P.; Gaich, T.; Köck, M.; Baran, P. S. *J. Am Chem. Soc.* **2007**, *129*, 12896.
Namba, K.; Takeuchi, K.; Kaihara, Y.; Oda, M.; Nakayama, A.; Nakayama, A.; Yoshida, M.; Tanino, K. *Nat. Commun.* **2015**, *6*, 8731.