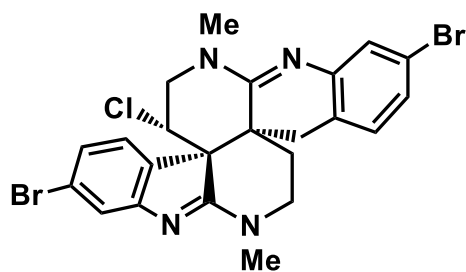
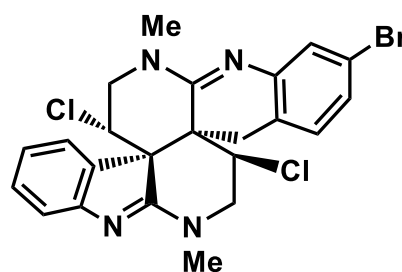


Enantioselective Total Syntheses of (–)-Caulamidine D and (–)-Isocaulamidine D and Their Absolute Configuration Reassignment

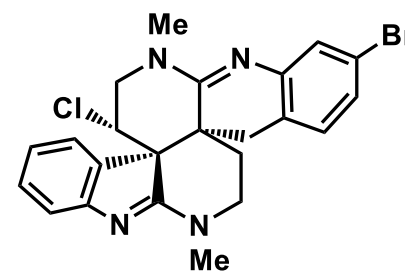
Haiyong Yu, Junhao Zhang, Dongxu Ma, Xiaotong Li, and Tao Xu*



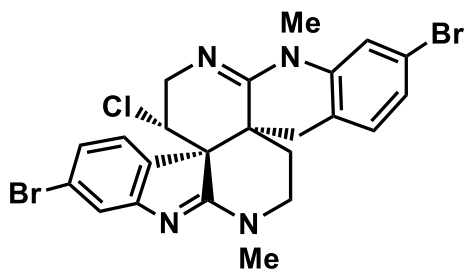
caulamidine B (1)



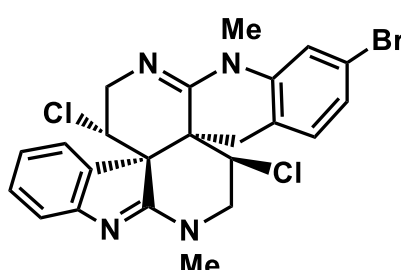
caulamidine C (3)



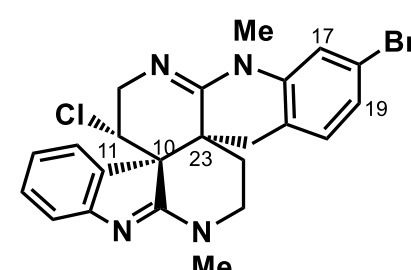
caulamidine D (5)



isocaulamidine B (2)

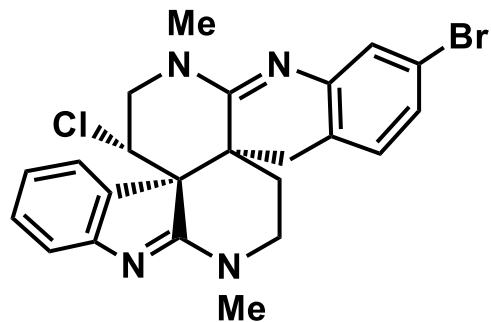


isocaulamidine C (4)



isocaulamidine D (6)

LG = OMs

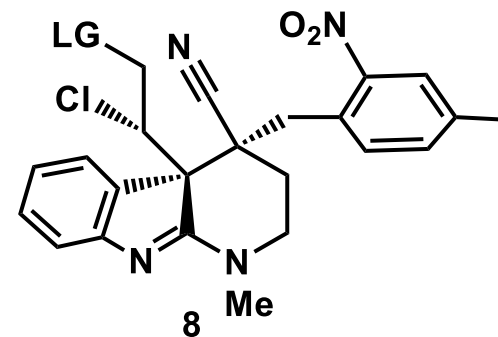


caulamidine D (5)

*stitching D-E-F
rings in one step*

*cascade
cyclization*

*divergent
methylation*

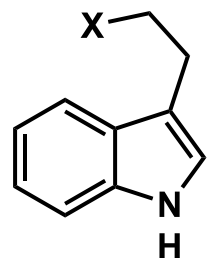
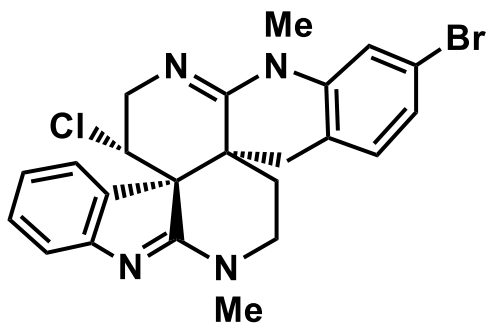


8

*C-ring
formation*

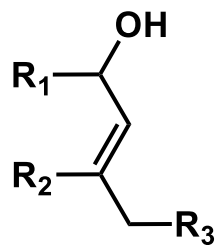
*Electrophilic
chlorination
/alkylation*

isocaulamidine D (6)



10

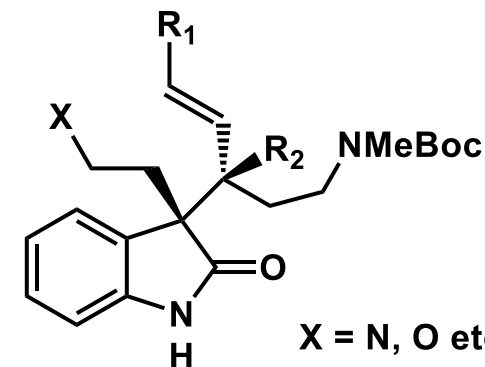
+



11

*Asymmetric
Meerwein/
Eschenmoser/
Claisen rearr.*

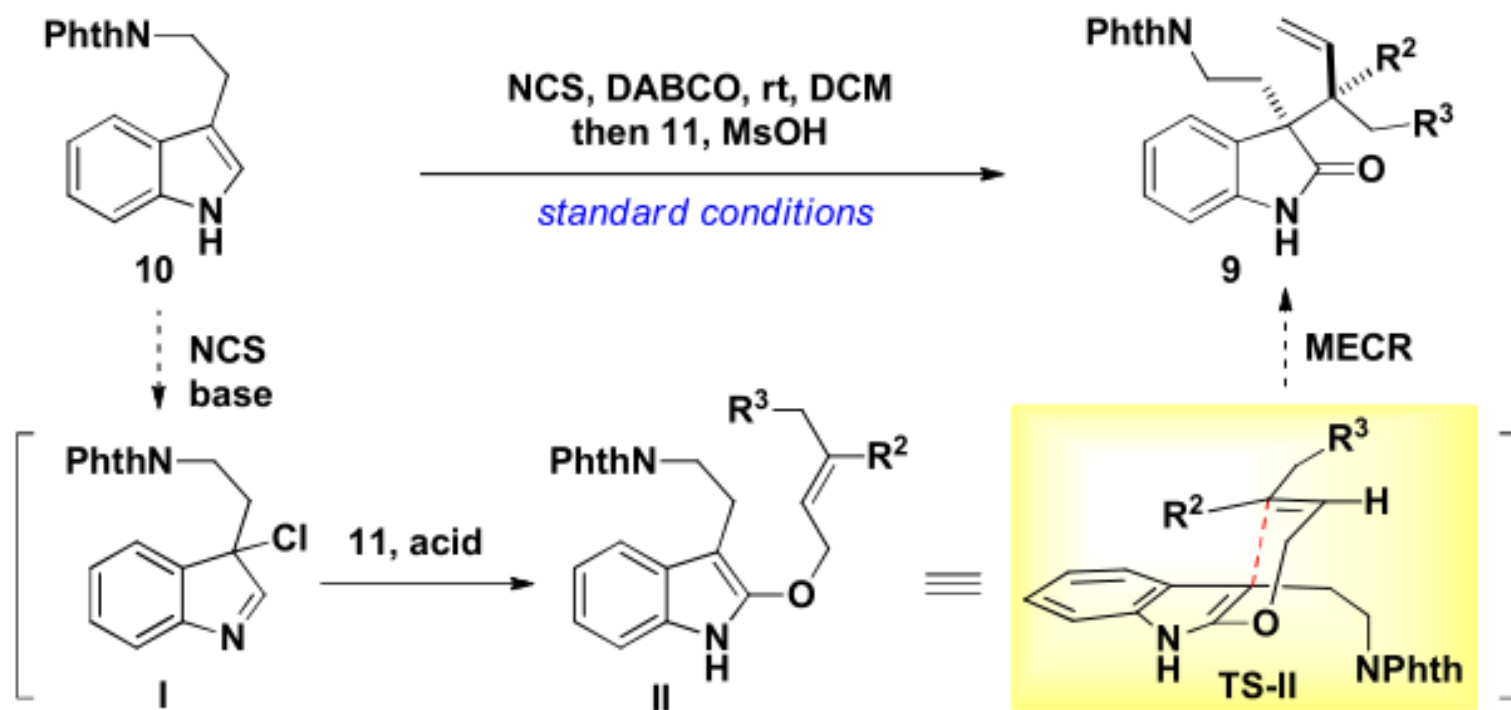
*vicinal
stereocenters
in one step*

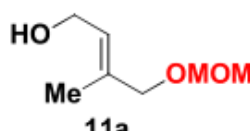
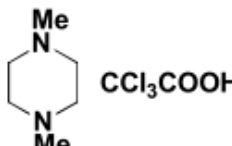
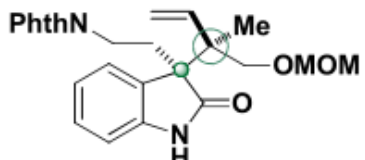
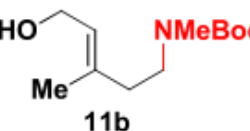
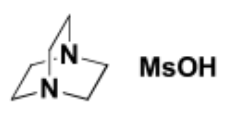
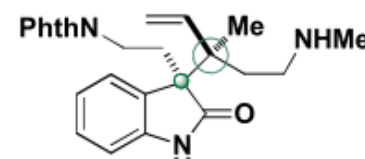
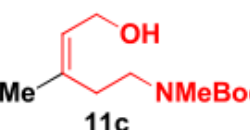
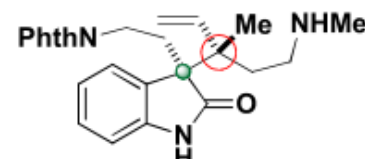
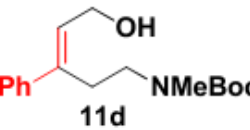
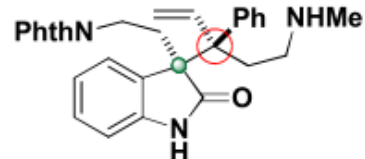
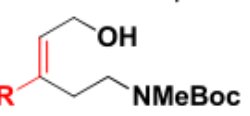
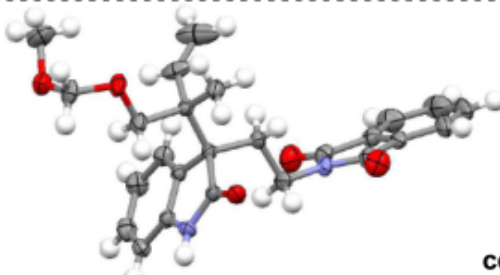


9

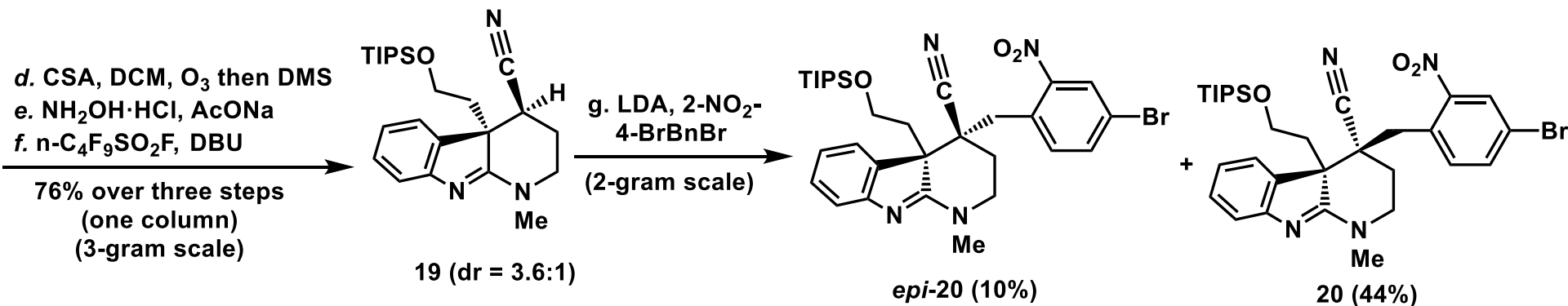
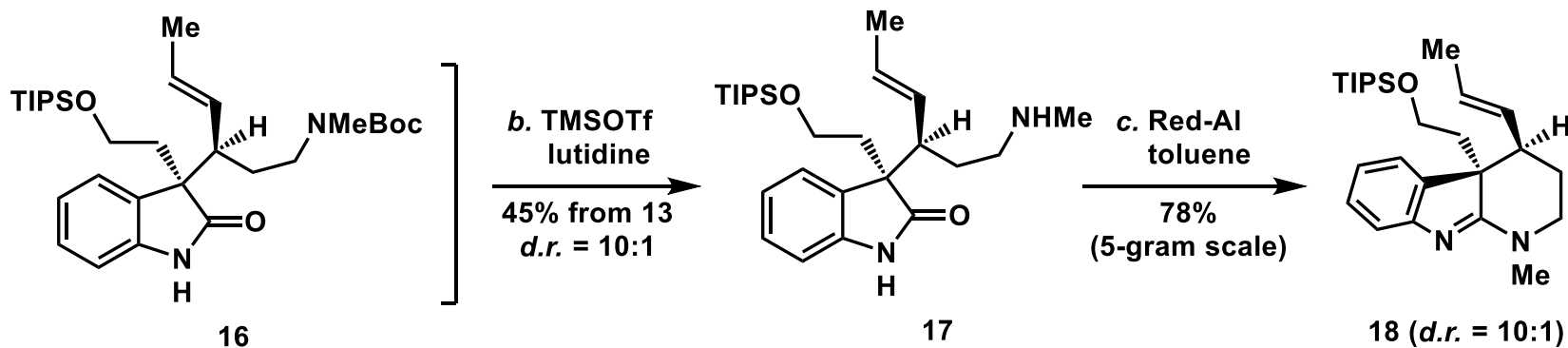
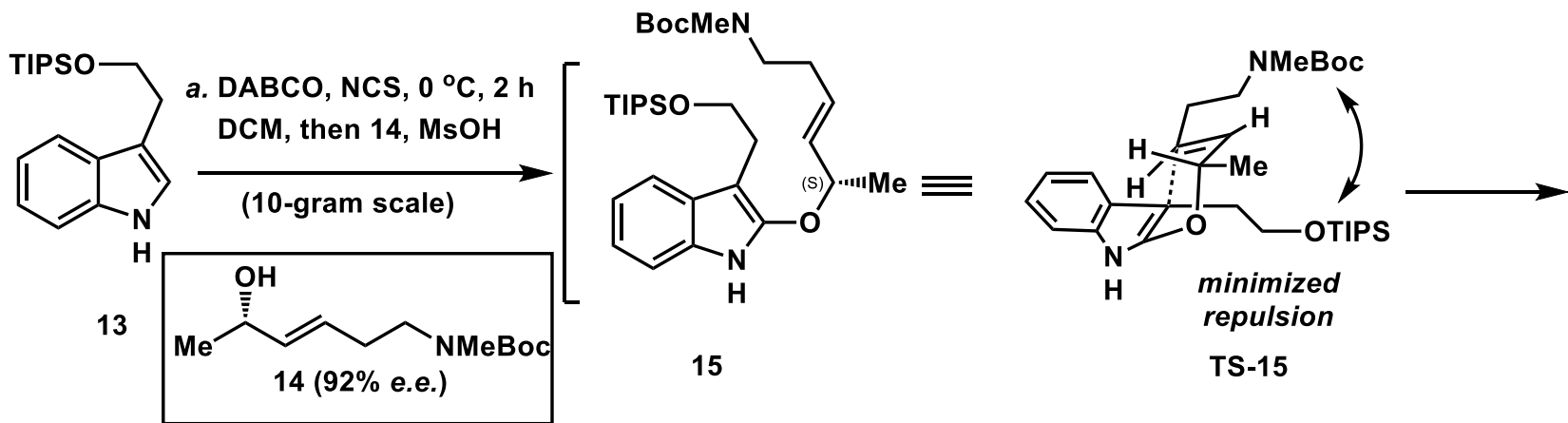
X = N, O etc

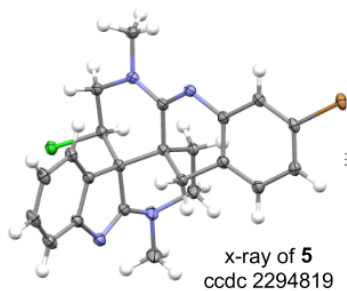
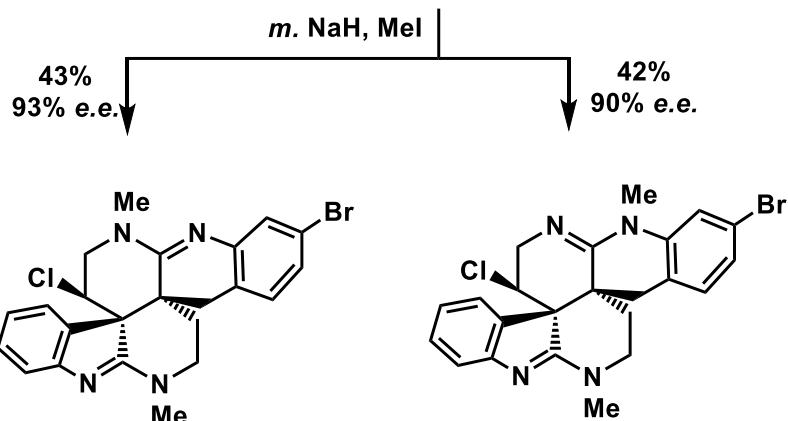
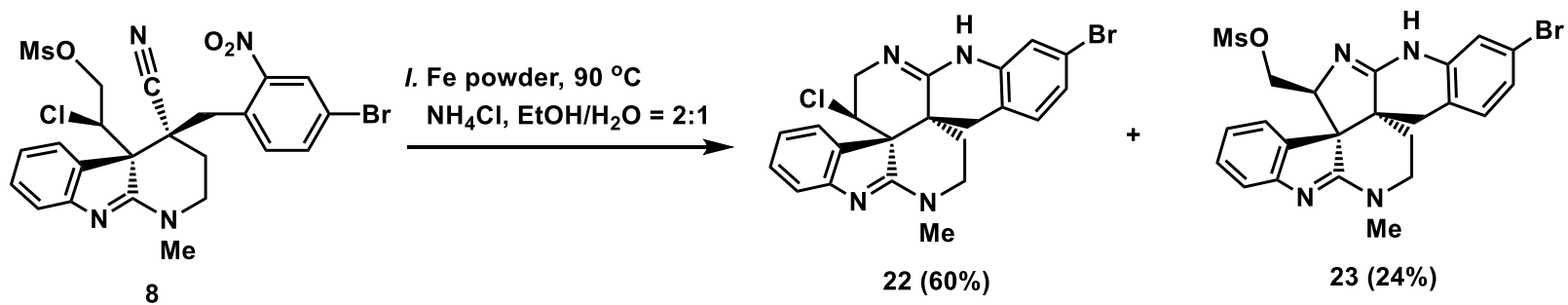
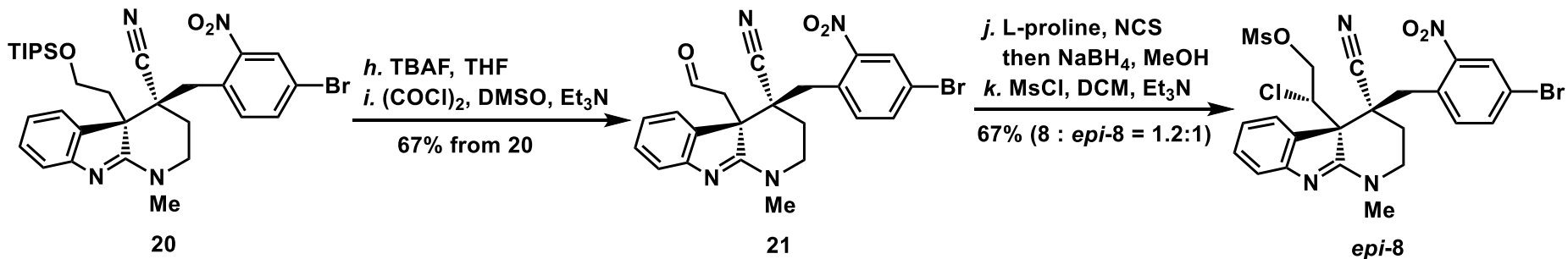
Scheme 1. Investigation of the Meerwein–Eschenmoser–Claisen Rearrangement



Entry ^a	Allyl alcohol	Base and acid	Products	Yield ^b
1	 11a	 CCl ₃ COOH	 9a (91%) dr>20:1	
2 ^c	 11b	 MsOH	 9b (63%) dr=14:1	
3 ^c	 11c (Z/E=11:1)	DABCO, MsOH	 9c (60%) dr=8:1	
4 ^c	 11d	DABCO, MsOH	 9d (56%) dr>20:1	
<i>unviable examples</i>  11e R=oNO ₂ Phenyl 11f R=oBrPhenyl 11g R=oNO ₂ Benzyl		 x-ray of 9a ccdc 2287959		

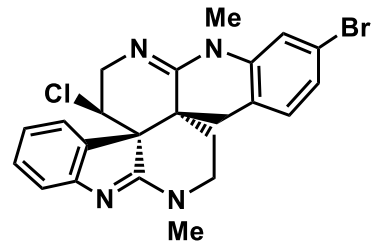
^aNCS (1.8 equiv) and base (1.0 equiv) were added sequentially to a DCM solution of **10** (1.6 equiv). Stirring was continued at 0 °C for 2 h before acid (0.25 equiv) and **11** (1.0 equiv) were added. ^bIsolated yields. ^cTFA was added during workup.





revised absolute configurations

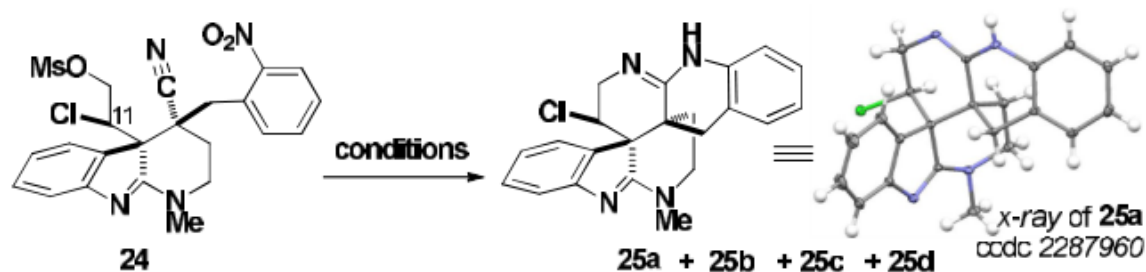
caulamidine D (**5**)



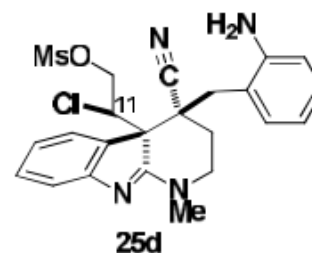
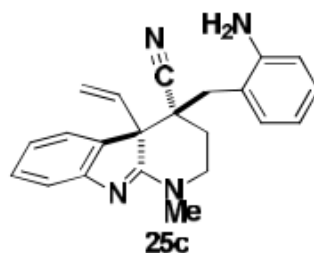
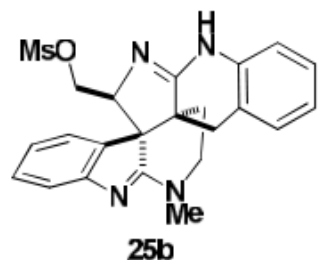
revised absolute configurations

isocaulamidine D (**6**)

Table 1. Selected Condition Optimization for the Cascade Cyclization^{a,b}



entry	conditions	temperature	25			
			a	b	c	d
1	Zn powder, NH ₄ Cl, EtOH/H ₂ O(2:1)	90 °C(2 h)	38%	16%	20%	3%
2	Fe powder, NH ₄ Cl, EtOH/H ₂ O(2:1)	90 °C(0.5 h)	43%	28%	0	24%
3	In powder, NH ₄ Cl, EtOH/H ₂ O(2:1)	90 °C(2 h)	25%	31%	3%	3%
4	Fe powder, HCl(6N), EtOH/H ₂ O(2:1)	90 °C(0.5 h)	23%	53%	0	3%
5	Fe powder, NH ₄ Cl, EtOH/H ₂ O(2:1)	90 °C(2 h)	49%	16%	0	3%
6	Fe powder, NH ₄ Cl, EtOH/H ₂ O(2:1)	90 °C(3 h)	53%	24%	0	0
7	Fe powder, NH ₄ Cl, EtOH/H ₂ O(2:1)	90 °C(5 h)	34%	13%	0	0
8	B ₂ (OH) ₄ , 4,4'-bipyridine, DMF	rt (10 mins)	0	0	0	54%



^aTo the EtOH (0.5 mL) and NH₄Cl(aq) (0.25 mL) solution containing 24 (0.06 mmol, 1 equiv) was added metal powder (4 equiv) at room temperature, and the mixture was stirred at 90 °C for 2 h. ^bIsolated yields are reported.

