Enantioselective Total Synthesis of (–)-Caulamidine A
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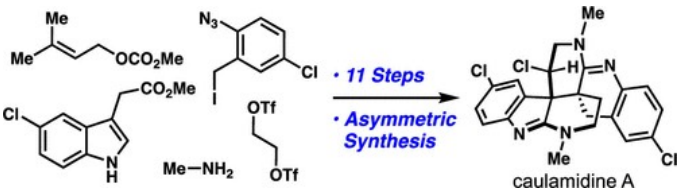
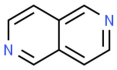


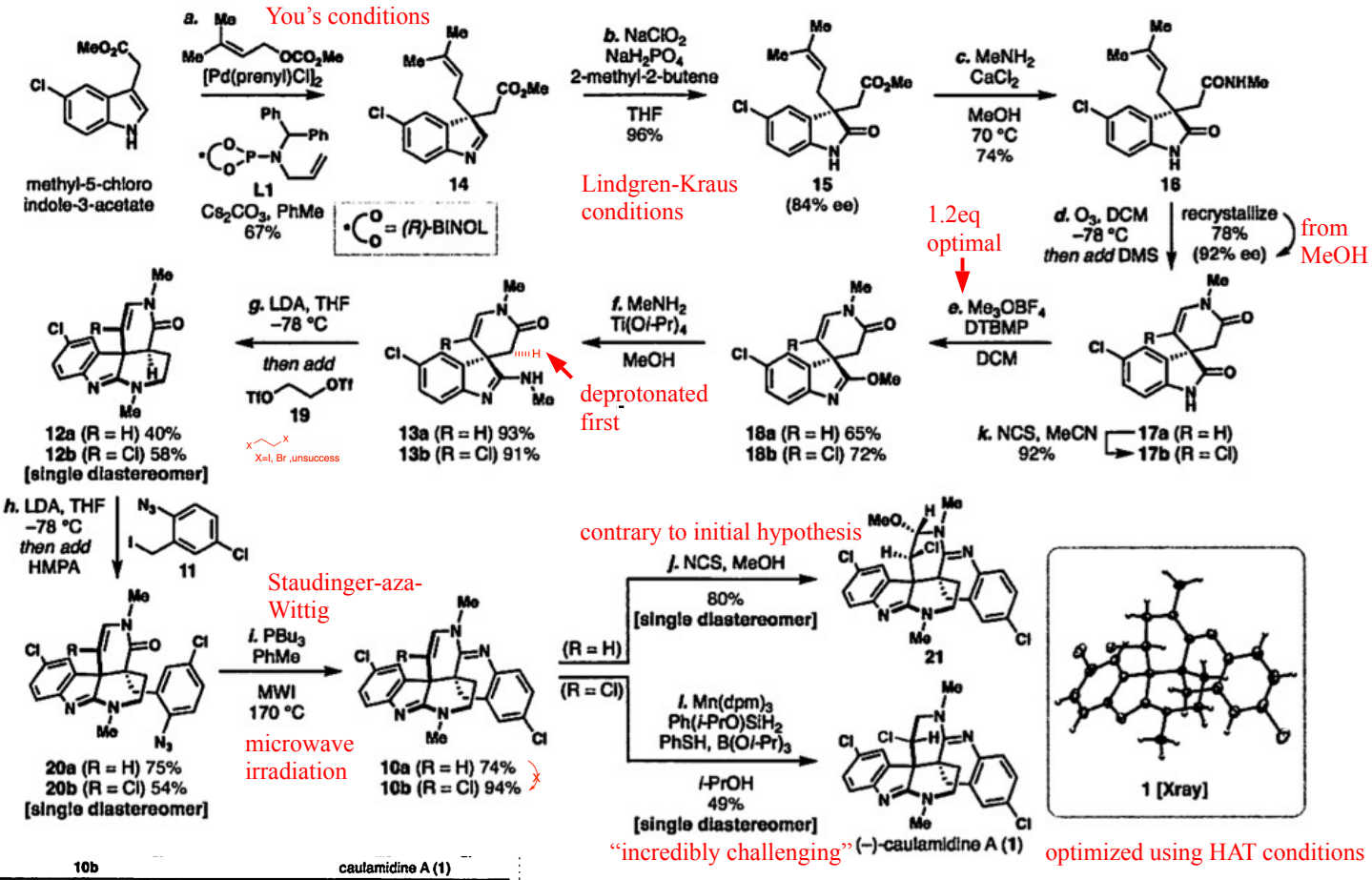
neopentylic stereocentor

ketone-amidine annulation


2,6-Naphthyridine

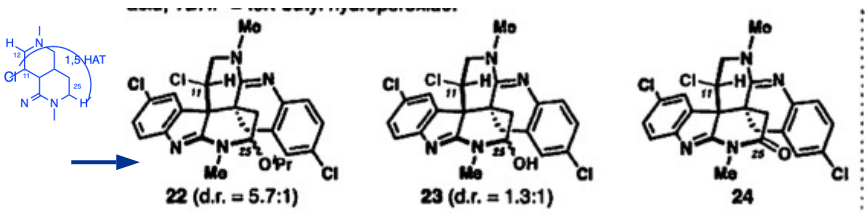
DTBMP

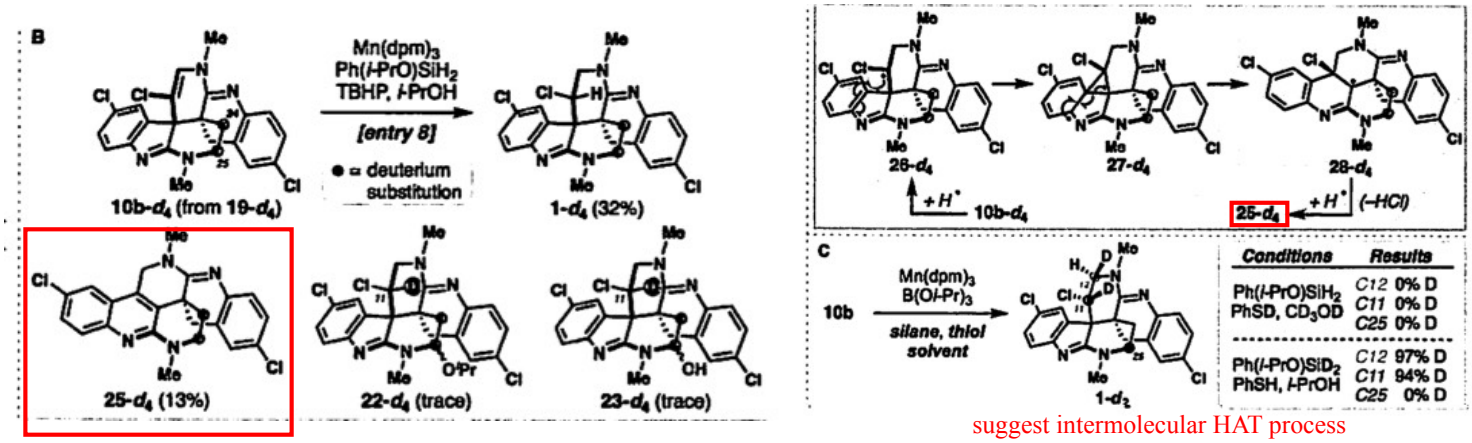
Scheme 1. Asymmetric Total Synthesis of Caulamidine A (1)[a]



Entry	Conditions	Reaction Products[a]
1	TFA, Et_3SiH, DCM	10b
2	H_2, PtO_2, AcOH/EtOAc	10b, 9 (14%), 1 (6%)
3	$Fe_2(ox)_3$, $NaBH_4$, EtOH/H_2O	10b
4	$Co(acac)_2$, Et_3SiH, 1,4-CHD, TBHP, *n*-PrOH, air	10b
5	$Fe(acac)_3$, $PhSiH_3$, PhSH, EtOH	10b
6	$Mn(dpm)_3$, $PhSiH_3$, TBHP, *i*-PrOH	10b
7[b]	$Mn(dpm)_3$, $Ph(i\text{-}PrO)SiH_2$, TBHP, *i*-PrOH	10b, 1 (trace)
8[c]	$Mn(dpm)_3$, $Ph(i\text{-}PrO)SiH_2$, TBHP, *i*-PrOH	10b (21%), 1 (15%), 22 (16%), 23 (9%), 24 (7%)
9[d]	$Mn(dpm)_3$, $Ph(i\text{-}PrO)SiH_2$, PhSH, *i*-PrOH	10b (62%), 1 (12%)
10[e]	$Mn(dpm)_3$, $Ph(i\text{-}PrO)SiH_2$, PhSH, $B(O\text{-}i\text{-}Pr)_3$, *i*-PrOH	10b (24%), 1 (49%)[f]

[a]Yields determined by ^1H NMR analysis. [b]Mn^{III} (5 mol%), silane (2 equiv.), TBHP (2 equiv.). [c]Mn^{III} (2 equiv.), silane (4 equiv.), TBHP (2 equiv.). [d]Mn^{III} (2 equiv.), silane (2 equiv.), PhSH (2 equiv.). [e]Mn^{III} (10 equiv.), silane (10 equiv.), PhSH (10 equiv.), $B(O\text{-}i\text{-}Pr)_3$ (2 equiv.), with *aq.* NH_4OH workup. [f]Isolated yield. TFA = trifluoroacetic acid, TBHP = tert-butyl hydroperoxide.





suggest intermolecular HAT process