Enantioselective Total Syntheses of Vallesamidine and Schizozygane Alkaloids

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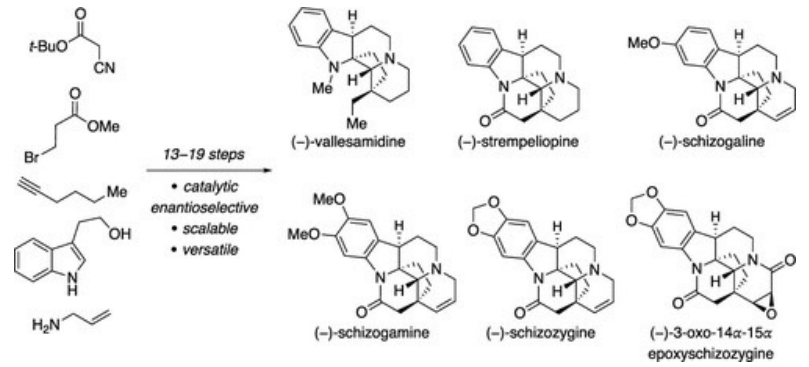
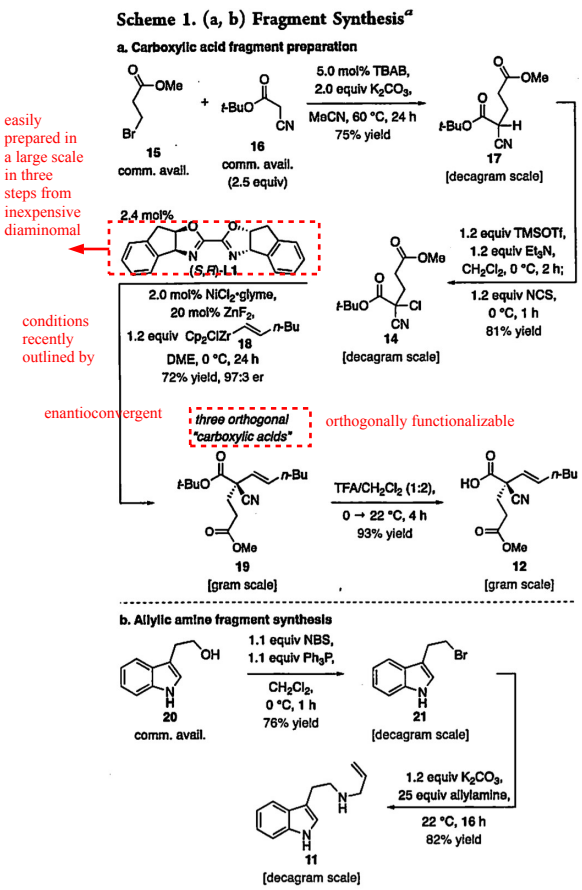
consist of a cyclase phase, followed by an oxidoreductase phase (vs the classic oxidase phase)



Scheme 1. (a, b) Fragment Synthesis[a]



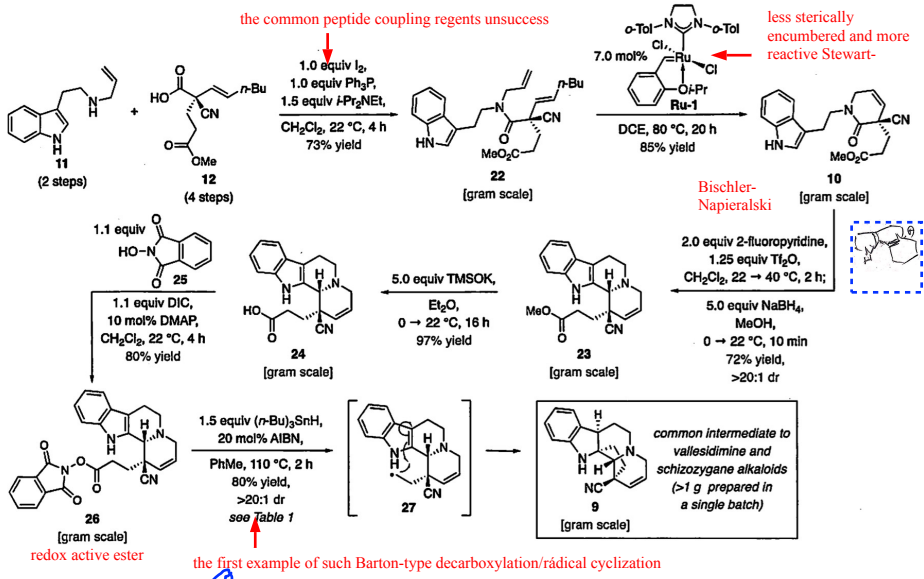
easily prepared in a large scale in three steps from inexpensive diaminomal

conditions recently outlined by

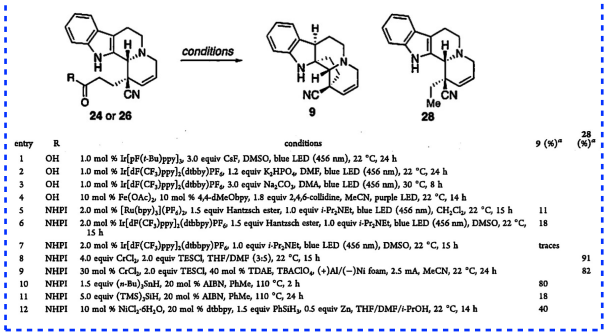
enantioconvergent

orthogonally functionalizable

Scheme 2. Cyclase Phase for the Preparation of the Common Intermediate to Vallesamidine and Schizozygane Alkaloids[a]

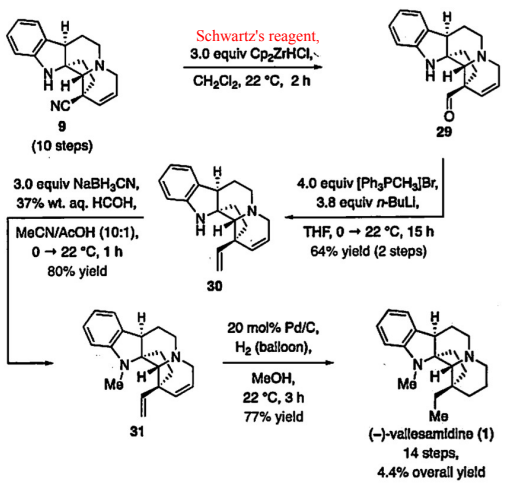


the first example of such Barton-type decarboxylation/rádical cyclization



entry	R	conditions	9 (%)[a]	28 (%)[a]
1	OH	1.0 mol % Ir[pF(t-Bu)ppy]$_3$, 3.0 equiv CsF, DMSO, blue LED (456 nm), 22 °C, 24 h		
2	OH	1.0 mol % Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$, 1.2 equiv K$_2$HPO$_4$, DMF, blue LED (456 nm), 22 °C, 24 h		
3	OH	1.0 mol % Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$, 3.0 equiv Na$_2$CO$_3$, DMA, blue LED (456 nm), 30 °C, 8 h		
4	OH	10 mol % Fe(OAc)$_2$, 10 mol % 4,4-dMeObpy, 1.8 equiv 2,4,6-collidine, MeCN, purple LED, 22 °C, 14 h		
5	NHPI	2.0 mol % [Ru(bpy)$_3$](PF$_6$)$_2$, 1.5 equiv Hantzsch ester, 1.0 equiv i-Pr$_2$NEt, blue LED (456 nm), CH$_2$Cl$_2$, 22 °C, 15 h	11	
6	NHPI	2.0 mol % Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$, 1.5 equiv Hantzsch ester, 1.0 equiv i-Pr$_2$NEt, blue LED (456 nm), DMSO, 22 °C, 15 h	18	
7	NHPI	2.0 mol % Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$, 1.0 equiv i-Pr$_2$NEt, blue LED (456 nm), DMSO, 22 °C, 15 h	traces	
8	NHPI	4.0 equiv CrCl$_2$, 2.0 equiv TESCl, THF/DMF (3:5), 22 °C, 15 h		91
9	NHPI	30 mol % CrCl$_2$, 2.0 equiv TESCl, 40 mol % TDAE, TBACIO$_4$, (+)Al/(−)Ni foam, 2.5 mA, MeCN, 22 °C, 24 h		82
10	NHPI	1.5 equiv (n-Bu)$_3$SnH, 20 mol % AIBN, PhMe, 110 °C, 2 h	80	
11	NHPI	5.0 equiv (TMS)$_3$SiH, 20 mol % AIBN, PhMe, 110 °C, 24 h	18	
12	NHPI	10 mol % NiCl$_2$·6H$_2$O, 20 mol % dtbbpy, 1.5 equiv PhSiH$_3$, 0.5 equiv Zn, THF/DMF/i-PrOH, 22 °C, 14 h	40	

Scheme 3. Oxidoreductase Phase for Vallesamidine[a]



Scheme 7. (a–c) Second-Generation Oxidoreductase Phase for Schizozygane Alkaloids[a]