# Concise Syntheses of Lycojapomine Alkaloids Enabled by Radical Dearomatization of a Pyrrole

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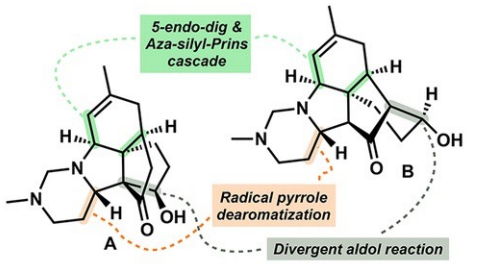
J. Am. Chem. Soc. 2025, 147, 20200-20204

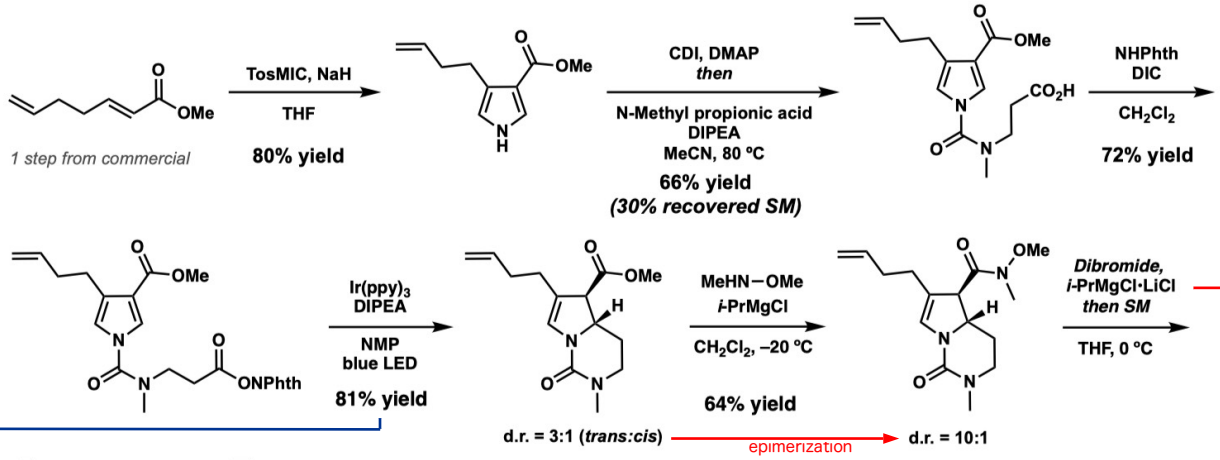
a photo-induced radical cyclization to selectively dearomatize a pyrrole

a silver-catalyzed cyclization cascade to annulate two rings and assemble the core carbon framework in a

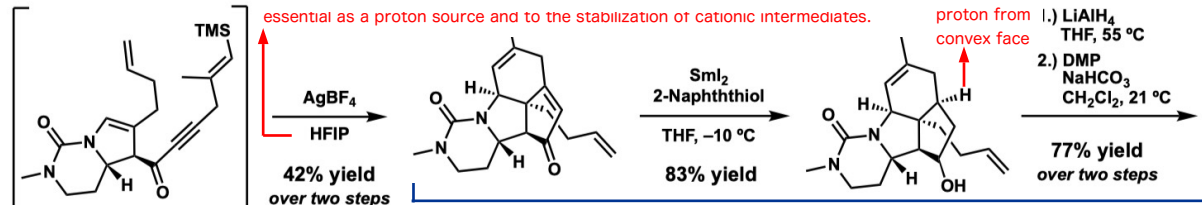



**Lycojapomine Alkaloids** • First reported total syntheses

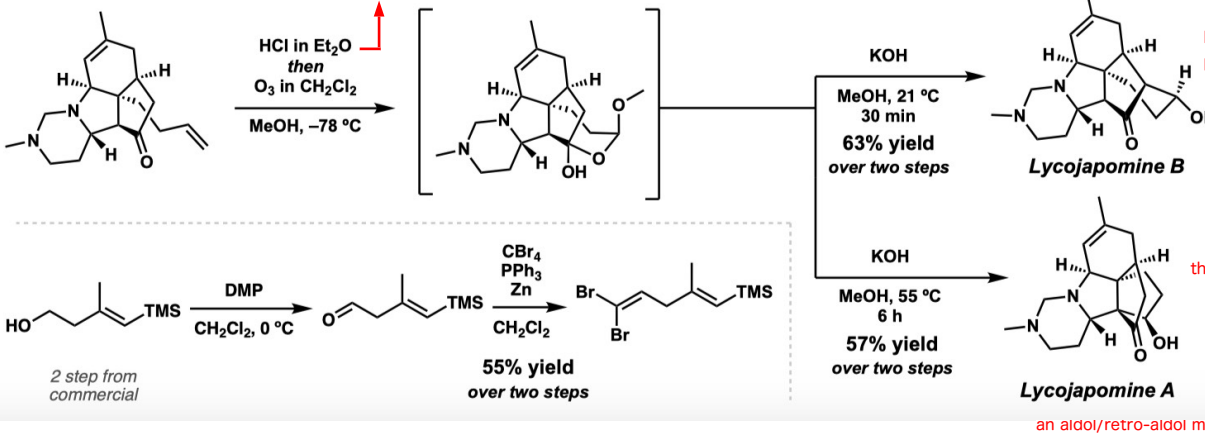
• No protecting groups used • 13 steps from commercial starting material



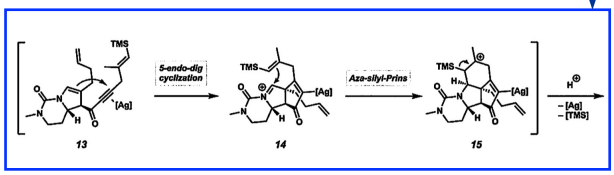

essential as a proton source and to the stabilization of cationic intermediates.



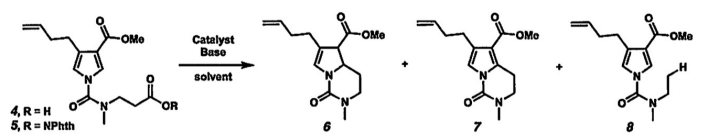

due to susceptibility of the hexahydropyrimidine to oxidation, HCl salt was used




an aldol/retro-aldol mechanism




three carbon-carbon bonds and two stereocenters,




| Entry | Catalyst | Additive | Solvent | 6 (yield in %) | 7 (yield in %) | 8 (yield in %) |
|---|---|---|---|---|---|---|
| 1 (R=H) | Ir[dF(CF3)ppy)]2(dtbbpy)PF6 | K2HPO4 | DMF | - | 5 | - |
| 2[a] | Fe(NO3)3 · 9 H2O (5 mol %) di(2-picolyl)amine (6.1 mol %) | TRIP disulfide (5 mol%), Na2CO3 (0.1 equiv) | DCE: H2O (1:1) | - | 25 | 25 |
| 3[b] (R=NPhth) | Eosin Y (10 mol %) | DIPEA (2.5 equiv) | CH2Cl2 | - | 10 | - |
| 4[c] | Ni(acac)2 (2.0 equiv) | Zn (50 equiv), LiCl (20 equiv), 50°C | DMF | - | - | - |
| 5[c] | Ru(bpy)3(PF6)2 | HE (1.5 equiv), DIPEA (2.0 equiv) | CH2Cl2 | 11 | 6 | 15 |
| 6[c] | Ru(bpy)3(PF6)2 | HE (1.5 equiv) | CH2Cl2 | 1 | 8 | 22 |
| 7[c] | Ru(bpy)3(PF6)2 | DIPEA (2.0 equiv) | CH2Cl2 | 10 | 7 | 11 |
| 8[c] | Ru(bpy)3(PF6)2 | DIPEA (2.0 equiv) | MeCN | 8 | 12 | 10 |
| 9[c] | Ru(bpy)3(PF6)2 | DIPEA (2.0 equiv) | DMF | - | - | - |
| 10[c] | Ru(bpy)3(PF6)2 | DIPEA (2.0 equiv) | DMA | 11 | 24 | 12 |
| 11[c] | Ru(bpy)3(PF6)2 | DIPEA (2.0 equiv) | DMSO | 18 | 32 | 11 |
| 12[c] | Ru(bpy)3(PF6)2 | DIPEA (2.0 equiv) | NMP | 15 | 23 | 13 |
| 13[c] | Ru(bpy)3(PF6)2 | Et3N (2.0 equiv) | DMSO | 10 | 17 | 5 |
| 14[c] | Ru(bpy)3(PF6)2 | Et3N (10.0 equiv) | DMSO | 14 | 24 | 8 |
| 15[c] | Ir(dtbbpy)(ppy)2PF6 | Et3N (5.0 equiv) | DMSO | 25 | 20 | 5 |
| 16[c] | Ir(dtbbpy)(ppy)2PF6 | DIPEA (10.0 equiv) | DMSO | 42[d] | 35 | 4 |
| 17[c] | Ir(ppy)3 | DIPEA (10.0 equiv) | DMSO | 53[d] | 33 | 2 |
| 18[c] | Ir(ppy)3 | DIPEA (10.0 equiv) | NMP | 81 | 10 | 3 |

Reactions were performed with 10 mg of starting material. Yield determined by 1H-NMR with internal standard. [a]Irradiated with purple LED (390 nm); [b]Irradiated with CFL; [c]1 mol % catalyst used, irradiated with blue LED (450 nm); [d]200 mg scale, isolated yield, d.r. = 3:1.

HE: Hantzsch ester

the redox potential of the photocatalyst determined the reaction

Ir(PPY)3: possesses one of the lower oxidation potentials

DMSO is poorly miscible with DIPEA

can be activated at much lower reduction potentials, possibly

**Scheme S2**: Consideration of pathways for annulation