Divergent Enantioselective Total Synthesis of (−)-Ajmalicine, (+)-Mayumbine, and (−)-Roxburghine C

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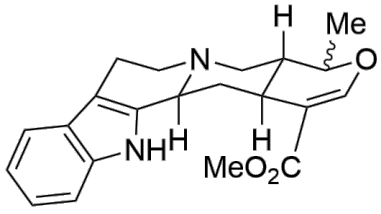
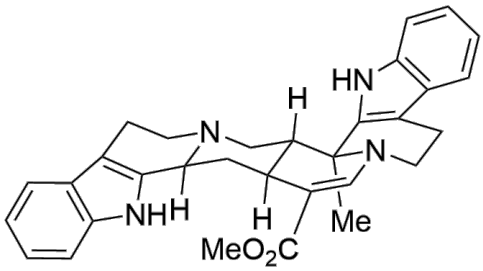
Heteroyohimbines, a subfamily of monoterpene indole alkaloids, display a range of intriguing bioactivities. In line with our ongoing interest in developing unified strategies for the synthesis of indole alkaloids, including bisindolic natural products, we developed a divergent enantioselective total synthesis of (−)-ajmalicine, (+)-mayumbine, and (−)-roxburghine C. The synthesis employs Franzén's organocatalytic reaction between *N*-acetoacetyl tryptamine and (*E*)-5-hydroxypent-2-enal to generate a functionalized pentacyclic compound with high diastereo- and enantioselectivity. This intermediate serves as a versatile platform for accessing the three heteroyohimbine alkaloids. Notably, a diastereoselective intramolecular Pictet–Spengler reaction of methyl ketone and chemoselective reduction of β-amidoester to β-enaminoester were exploited for the synthesis of (−)-roxburghine C.



(–)-ajmalicine, α-Me
(+)-mayumbine, β-Me



(–)-roxburghine C

[1] V. Goëlo, Q. Wang, J. Zhu, *Org. Lett.* **2025**, *27*, 13, 3326–3331.