Selective synthesis of an octacyclic fused scaffold via a one-pot oxidative dimerization reaction

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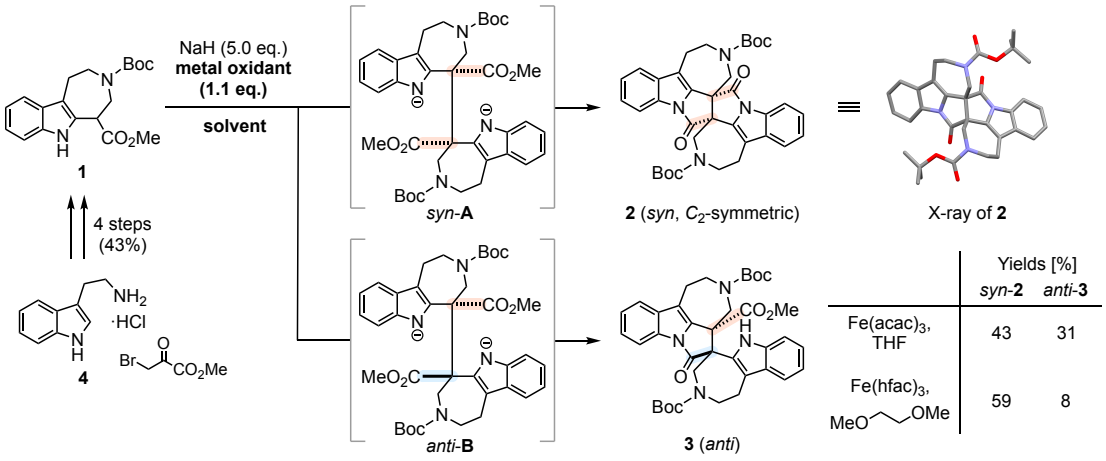
Synthetic approaches for constructing vicinal quaternary carbon centers remain a significant challenge. In this study, we developed a one-pot oxidative dimerization reaction of the azepinoindole scaffold **1**, which contains a methyl ester substituent at the adjacent carbon to the indole C2 position, enabling the formation of contiguous quaternary centers. This method facilitated the rapid and stereodivergent assembly of a C_2-symmetric octacyclic dimeric alkaloidal scaffold **1** (*syn*) and a septacyclic compound **2** (*anti*).

The dimerization precursor, azepinoindole scaffold **3**, was synthesized from tryptamine hydrochloride **4** in 4 steps. Treatment of **3** with an excess amount of NaH and $Fe(acac)_3$ allowed one-pot dimerization and subsequent lactam formations to furnish octacyclic **1** (43%) and heptacyclic product **2** (31%). X-ray analysis of crystalline *syn*-**1** revealed its C_2-symmetric dimeric structure with installation of vicinal quaternary carbon centers. Mechanistically, this one-pot reaction likely proceeds through single-electron oxidation of the enolate, followed by radical-mediated C–C bond formation to generate both intermediates *syn*-**A** and *anti*-**B**, which then undergo lactam formation. Optimization studies showed that the use of $Fe(hfac)_3$ in dimethoxyethane significantly improved the yield of *syn*-**1** (59%) while suppressing the formation of *anti*-**2** (8%). Further investigations to improve the yield and diastereoselectivity of the dimerization as well as to expand the substrate scope, are ongoing and will be reported.



	Yields [%] *syn*-**2**	*anti*-**3**
$Fe(acac)_3$, THF	43	31
$Fe(hfac)_3$, MeO–OMe	59	8