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Biomimetic Synthesis of the IDO Inhibitors Exiguamine A and B
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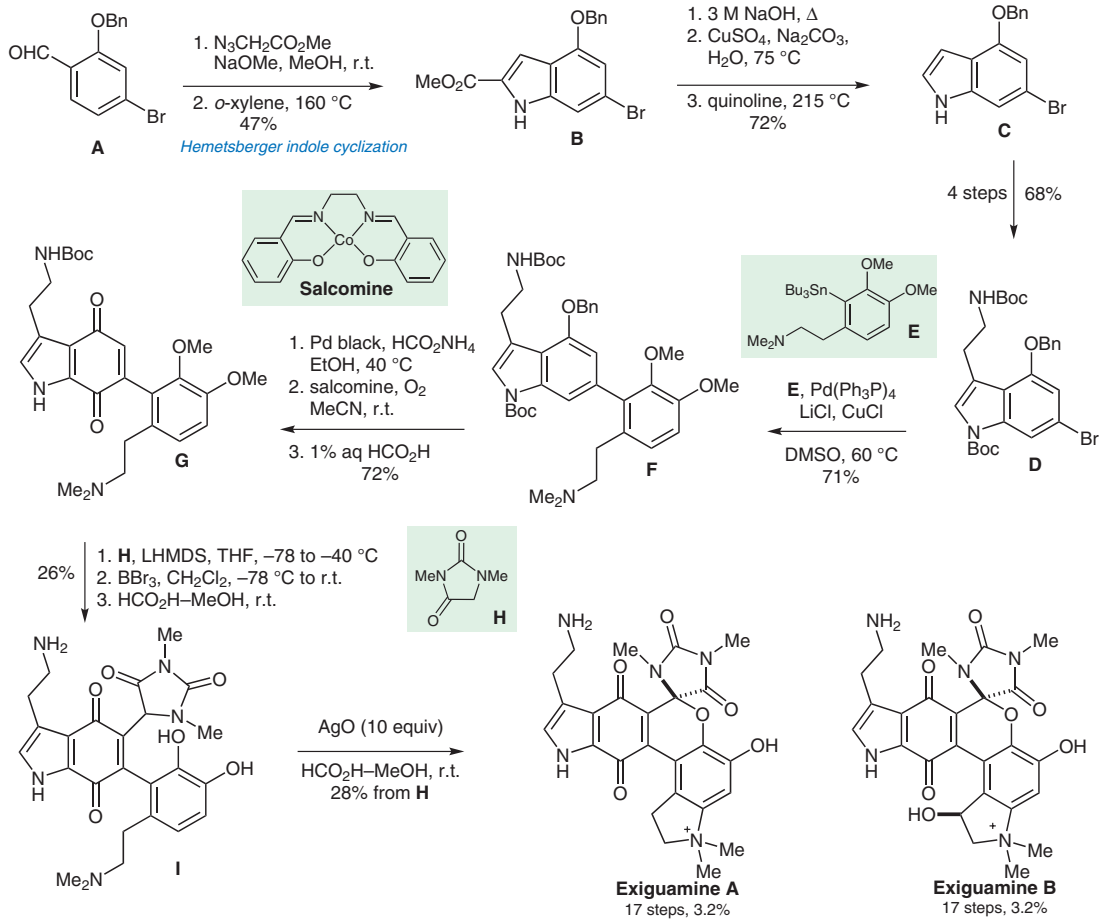
Synthesis of Exiguamine A



Significance: Exiguamine A is isolated from the marine sponge *Neopetrosia exigua* and is a potent inhibitor of indoleamine-2,3-dioxygenase, which in turn metabolizes tryptophan. This biomimetic synthesis relies on a cascade sequence involving intramolecular nucleophilic attack of a tertiary amine onto an *o*-quinone and tautomerization followed by an oxa-6π-electrocyclization (**I** → exiguamine A).

Comment: The phenol resulting from benzyl deprotection of **F** was subjected to salcomine oxidation which gave a 2.5:1 mixture of the regioisomeric *o*- and *p*-quinones, respectively (**F** → **G**). Upon treatment with 10 equivalents of AgO, **I** afforded exiguamine A, but with 20 equivalents of AgO exiguamine B was the main product. Treatment of exiguamine A with excess of AgO failed to give exiguamine B.

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