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Enantioselective, Protecting-Group-Free Total Synthesis of Sarpagine Alkaloids – A Generalized Approach
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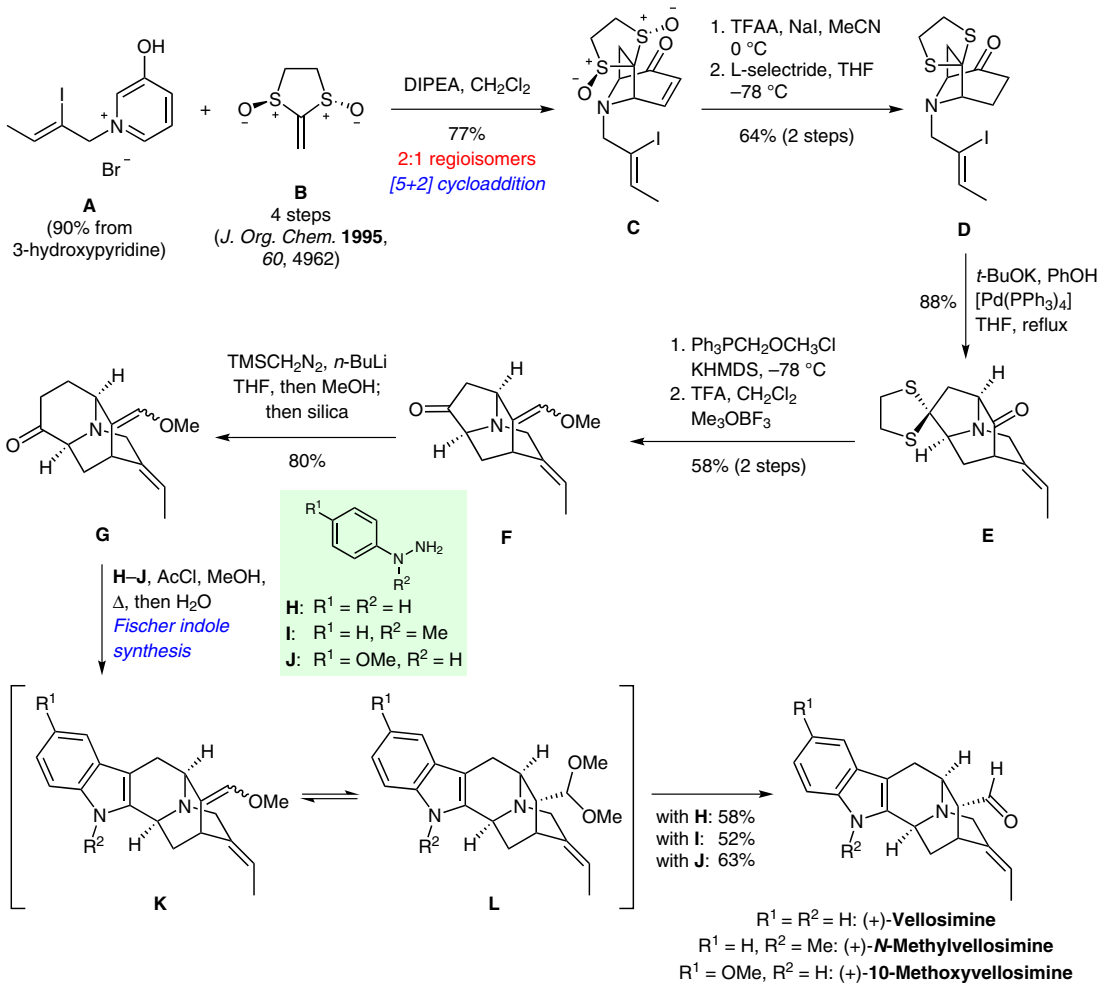
Synthesis of Sarpagine Alkaloids



Significance: The authors report the enantioselective total synthesis of three sarpagine indole alkaloids which were isolated from the plant family *Apocynaceae*. The route relies on a common intermediate **G**, which is impressively accessed using key features such as a [5+2] oxidopyridinium cycloaddition and a ring expansion. The three natural products were synthesized in only eight steps starting from known materials (12 steps from commercially available compounds).

Comment: The synthesis commenced with a [5+2] cycloaddition between oxidopyridinium salt **A** and Aggarwal's chiral ketene equivalent **B**, thus yielding the desired regioisomer **C** in a 2:1 ratio. Next, ketone **G** was accessed through an intramolecular palladium-catalyzed enolate coupling of **D**, followed by Wittig reaction, deprotection of the dithiolane, and ring expansion. The indole was introduced in the last step by a Fischer indole synthesis using phenylhydrazines with different substitution patterns to afford the three targets.

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