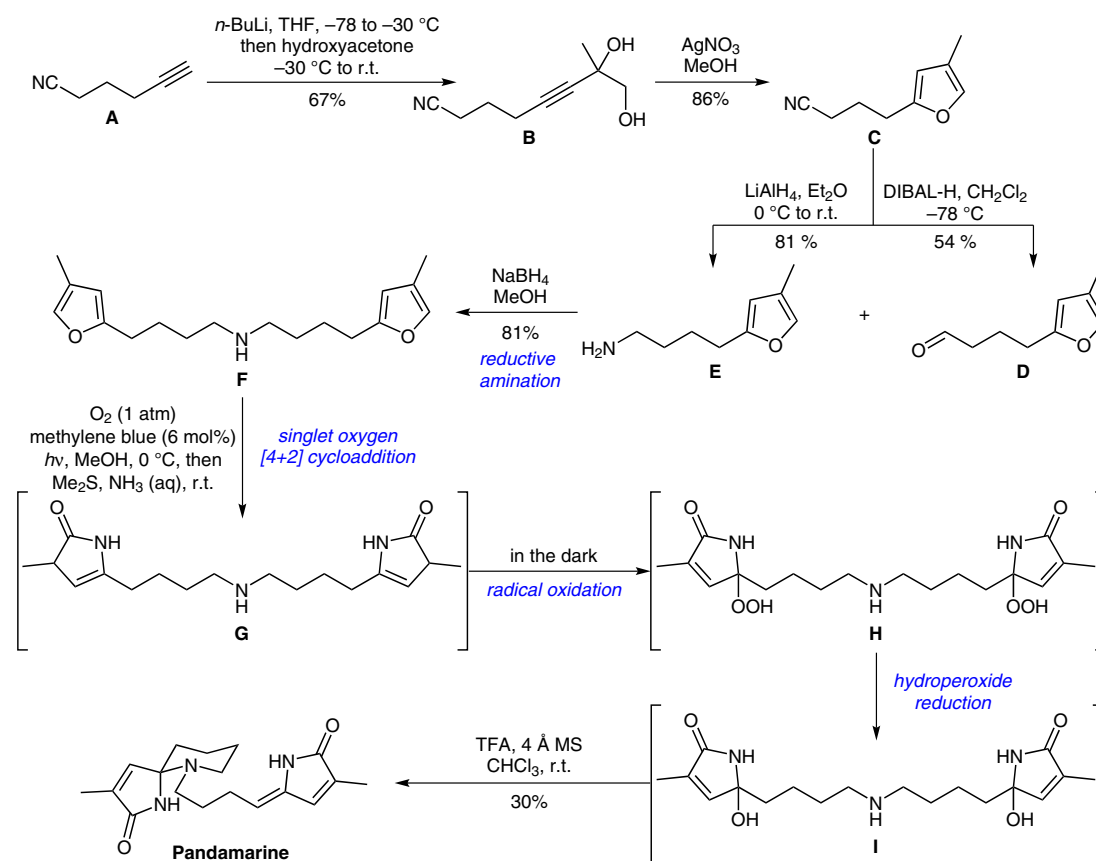


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First Total Synthesis of Pandamarine

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Total Synthesis of Pandamarine



Significance: The alkaloid pandamarine was isolated from leaves of the tropical plant *Pandanus amaryllifolius*, and features an interesting di-azaspiro[4.5] core. After the group's report of the oxidation of furans to 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones (*Angew. Chem. Int. Ed.* **2015**, *54*, 6283), they now disclose an elegant total synthesis of pandamarine relying on the double use of their methodology. Crucial to the success of the key transformation of bisfuran **F** to pandamarine is the dual role of methylene blue as both photosensitizer and redox catalyst.

Comment: Addition of excess alkyne **A** to hydroxyacetone furnished diol **B** which underwent silver-mediated cyclodehydration to furan **C**. Nitrile **C** was the precursor for both aldehyde **D** and amine **E**, which were coupled by reductive amination to give bisfuran **F**. In their key step, exposure of **F** to oxygen and methylene blue, followed by ammonia and dimethylsulfide gave intermediate bislactam **G**. In situ methylene blue catalyzed radical oxidation with triplet oxygen and hydroperoxide reduction then furnished intermediate **I**. Acid-catalyzed cyclization and elimination completed the synthesis of pandamarine in 30% yield.

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