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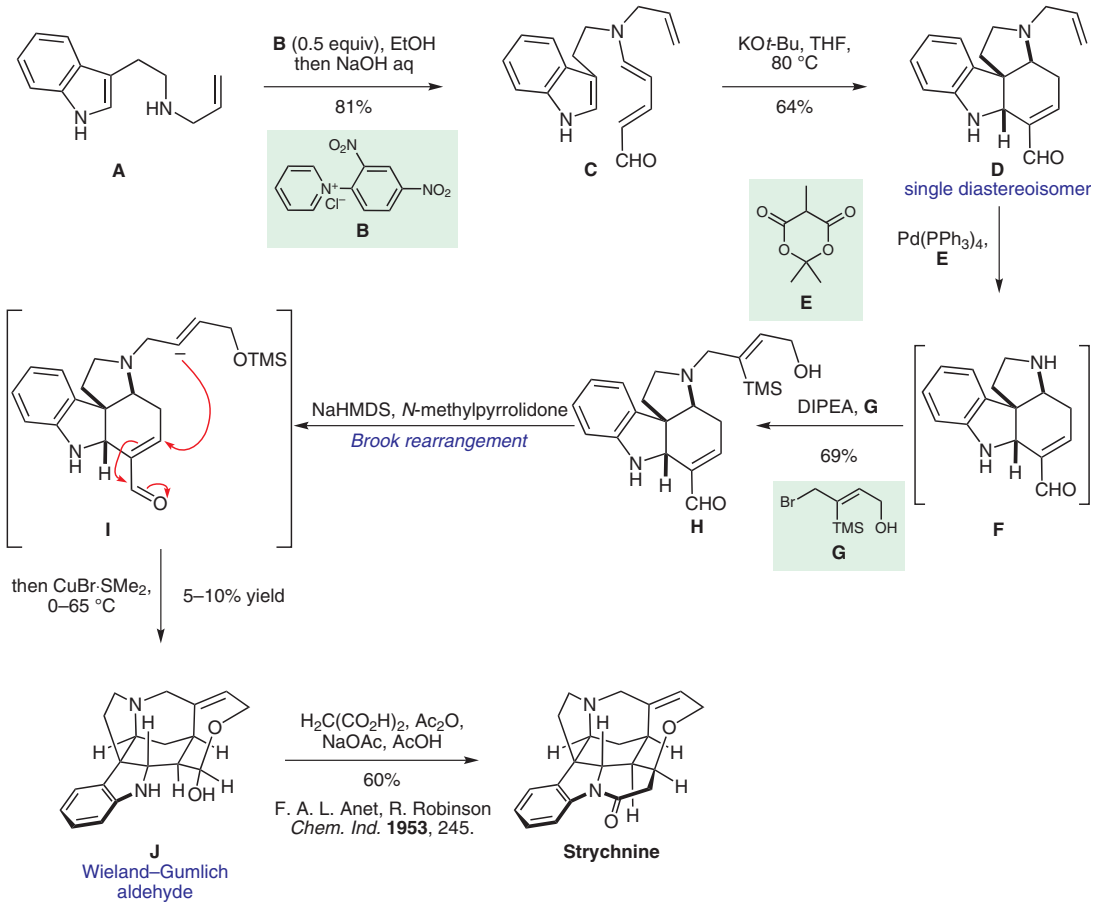
A Synthesis of Strychnine by a Longest Linear Sequence of Six Steps
Chem. Sci. **2011**, *2*, 649-651.

Synthesis of Strychnine



Significance: Strychnine is a highly toxic alkaloid isolated from seeds of the *Strychnos nux vomica* tree. It was first synthesized by Woodward and co-workers in 1954, and has since proved a popular target within the synthetic community. This approach is highly efficient and only requires six steps in the longest linear sequence.

Comment: The conversion of Zincke aldehyde **C** into tetracycle **D** via base-mediated cyclization proceeded efficiently and in good yield (D. B. Martin, C. Vanderwal *J. Am. Chem. Soc.* **2009**, *131*, 3472). Alkylation of bromide **G** (three steps from 1,4-butynediol) with amine **F** provided alcohol **H**. This underwent a 1,4-Brook rearrangement in situ, which upon treatment with a copper(I) source provided the core of strychnine. Unfortunately, after extensive optimization, the yield remained low and the major byproduct was due to protodesilylation.

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Synfacts 2011, 5, 0463-0463 Published online: 15.04.2011
DOI: 10.1055/s-0030-1259793; **Reg-No.:** N02111SF