Synthesis of Strychnine

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A Synthesis of Strychnine by a Longest Linear Sequence of Six Steps

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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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