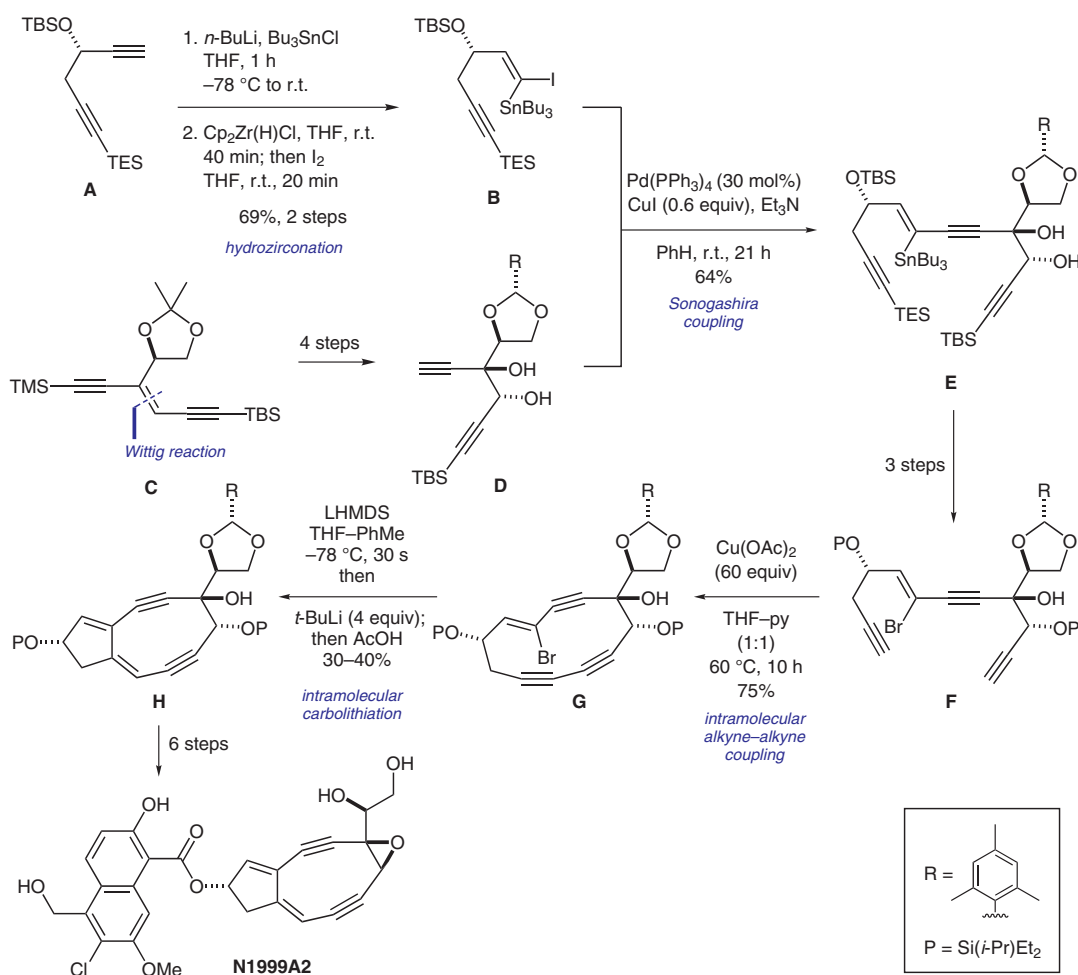


N. JI, H. O'DOWD, B. M. ROSEN, A. G. MYERS* (HARVARD UNIVERSITY, CAMBRIDGE, USA)

Enantioselective Synthesis of N1999A2

J. Am. Chem. Soc. **2006**, *128*, 14825-14827.

Synthesis of N1999A2



Significance: N1999A2 is an enediyne antibiotic that damages DNA by radical means. Noteworthy in this synthesis is the deft use of mild organometallic processes and a carefully wrought protecting group strategy to accomplish construction of the very sensitive target.

Review: *Chemistry and Biology of the Enediyne Anticancer Antibiotics* K. C. Nicolaou, W.-M. Dai *Angew. Chem. Int. Ed.* **1991**, *30*, 1387-1530.

Comment: Treatment of bisalkyne **F** with Cu(OAc)₂ gave **G** via intramolecular alkyne-alkyne coupling. Addition of LHMDS followed by *t*-BuLi gave **H** via lithium-bromine exchange followed by intramolecular carbolithiation. This step suffered from poor scalability and all subsequent intermediates (including **K**) were unstable in neat form. Despite such adversity, N1999A2 was accessed in six further steps.

SYNFACTS Contributors: Philip Kocienski, Thomas Snaddon
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Key words

hydrozirconation

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