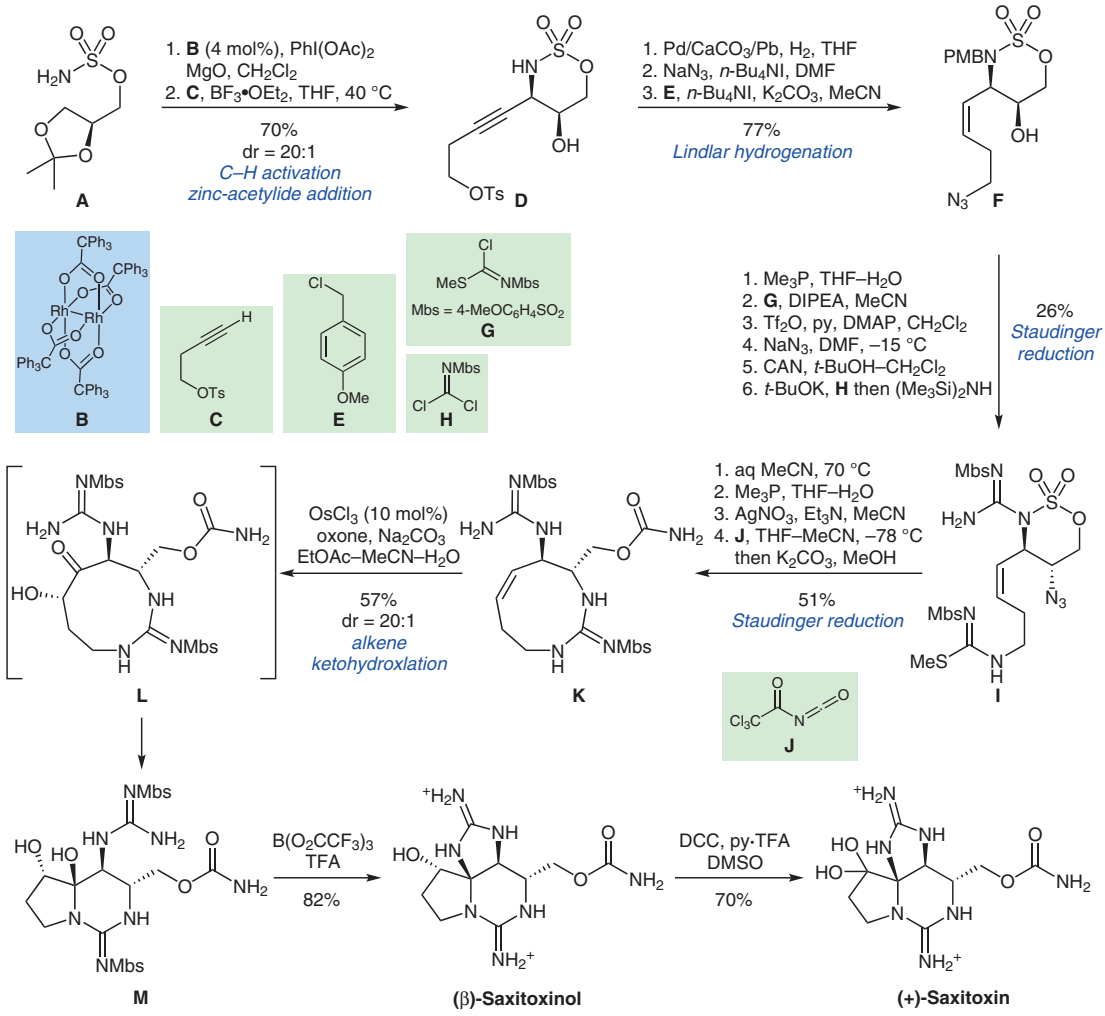
J. J. FLEMING, J. DU BOIS* (STANFORD UNIVERSITY, USA)

A Synthesis of (+)-Saxitoxin
J. Am. Chem. Soc. **2006**, *128*, 3926–3927, DOI: 10.1021/ja0608545.

Total Synthesis of (+)-Saxitoxin



Significance: In 2006, Du Bois and Fleming presented the enantioselective synthesis of (+)-saxitoxin, a paralytic agent isolated from oceanic red tides. The bioactivity of (+)-saxitoxin derives from the selective blockage of cations through Na^+ ion channels. It is a highly attractive target for total synthesis due to its tricyclic structure decorated with nitrogen and oxygen atoms.

Comment: The synthesis commences with the preparation of cyclic sulfamate **D** via Rh-catalyzed C–H activation followed by nucleophilic addition of the preformed zinc-acetylide species to N,O-acetal **A**. $AgNO_3$ initiates guanidine formation to form the nine-membered heterocycle **K** as a key intermediate. Alkene ketohydroxylation of **K** triggers the transannular cyclization to the 5/6 fused bicyclic structure **M**. From there, (β)-saxitoxinol and (+)-saxitoxin are accessed.

SYNFACTS Contributors: Erick M. Carreira, Sander Folkerts
Synfacts 2024, 20(07), 0677 Published online: 14.06.2024
DOI: 10.1055/s-0043-1774904; **Reg-No.:** C04924SF

Category
Synthesis of Natural Products

Key words
(+)-saxitoxin
(β)-saxitoxinol
C–H activation
zinc-acetylide addition
Lindlar hydrogenation
Staudinger reduction
alkene ketohydroxylation