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SYNFACTS Highlights in Current Synthetic Organic Chemistry

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Category

Synthesis of Natural Products and Potential Drugs

Key words

assembly-line synthesis

iterative homologation

(+)-kalkitoxin

(+)-hydroxyphthioceranic acid S. BALIEU, G. E. HALLETT, M. BURNS, T. BOOTWICHA, J. STUDLEY, V. K. AGGARWAL* (UNIVERSITY OF BRISTOL AND VERTEX PHARMACEUTICALS LIMITED, ABINGDON, UK) Toward Ideality: The Synthesis of (+)-Kalkitoxin and (+)-Hydroxyphthioceranic Acid by Assembly-Line Synthesis *J. Am. Chem. Soc.* **2015**, DOI: 10.1021/ja512875g.

Assembly-Line Synthesis of (+)-Kalkitoxin and (+)-Hydroxyphthioceranic Acid

Significance: The stepwise construction of carbon scaffolds following an iterative strategy with no functional group interconversions or purifications is very attractive. Aggarwal and co-workers showcase the power of boronic ester homologation with up to seven iterations in two enantioselective syntheses of (+)-kalkitoxin and (+)-hydrophthioceranic acid.

Comment: The chiral lithiated species **B** and **D** were derived from the respective enantiopure stannanes by treatment with s-BuLi. (Chloromethyl)lithium (**C**) was generated by lithium—halogen exchange of BrCH₂Cl or ICH₂Cl in the presence of the crude boronic esters. The yield of **H** corresponds to an impressive yield of 91% per iteration with excellent diastereo- and enantiocontrol.

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