Category

Synthesis of Natural Products and Potential Drugs

Key words

JNJ-A07

antiviral

indolines

M. VAN LOOCK*, J. NEYTS* ET AL. (JANSSEN PHARMACEUTICA, BEERSE AND KU LEUVEN, BELGIUM; GLOBAL VIRUS NETWORK (GVN), BALTIMORE, USA)

A Pan-serotype Dengue Virus Inhibitor Targeting the NS3–NS4B Interaction

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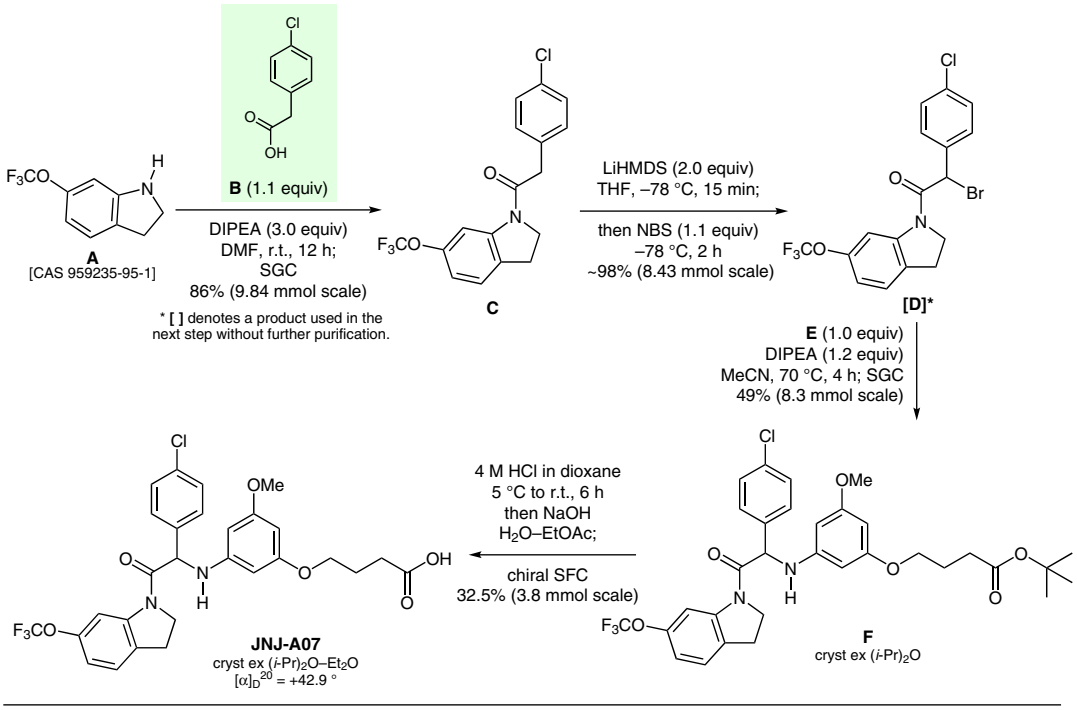
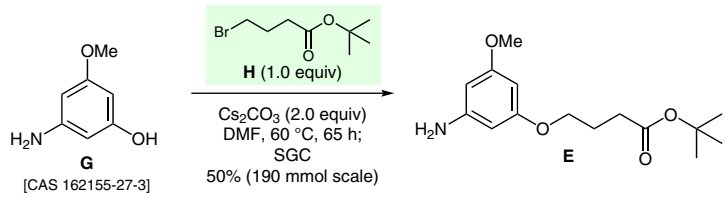
Synthesis of Dengue Virus Inhibitor JNJ-A07



Synthesis of fragment E:



Significance: Dengue is a mosquito-borne disease that afflicts 96 million people annually, making it one of the top ten global health threats. There are no antiviral agents available to prevent or treat dengue. A dengue virus inhibitor (JNJ-A07) has been discovered that exerts nanomolar to picomolar activity against a panel of 21 clinical isolates. JNJ-A07 blocks the interaction between two viral proteins (NS3 and NS4B), thus revealing a previously undescribed mechanism of antiviral action.

Comment: The synthesis of JNJ-A07 depicted is taken from an associated patent (WO **2017** 167951 A1, Example 4B). This simple and conventional approach delivered 24 substituted indoline analogues which included the enantiomers arising from the single stereogenic center. These were separated by chiral supercritical fluid chromatography. The dextrorotatory enantiomer of unknown absolute configuration corresponds to JNJ-A07.

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