Category

Synthesis of Natural Products and Potential Drugs

Key words

spirotryprostatin A

Mizoroki–Heck reaction

diketopiperazines

spirocycles

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Stereoselective Synthesis of Spirotryprostatin A
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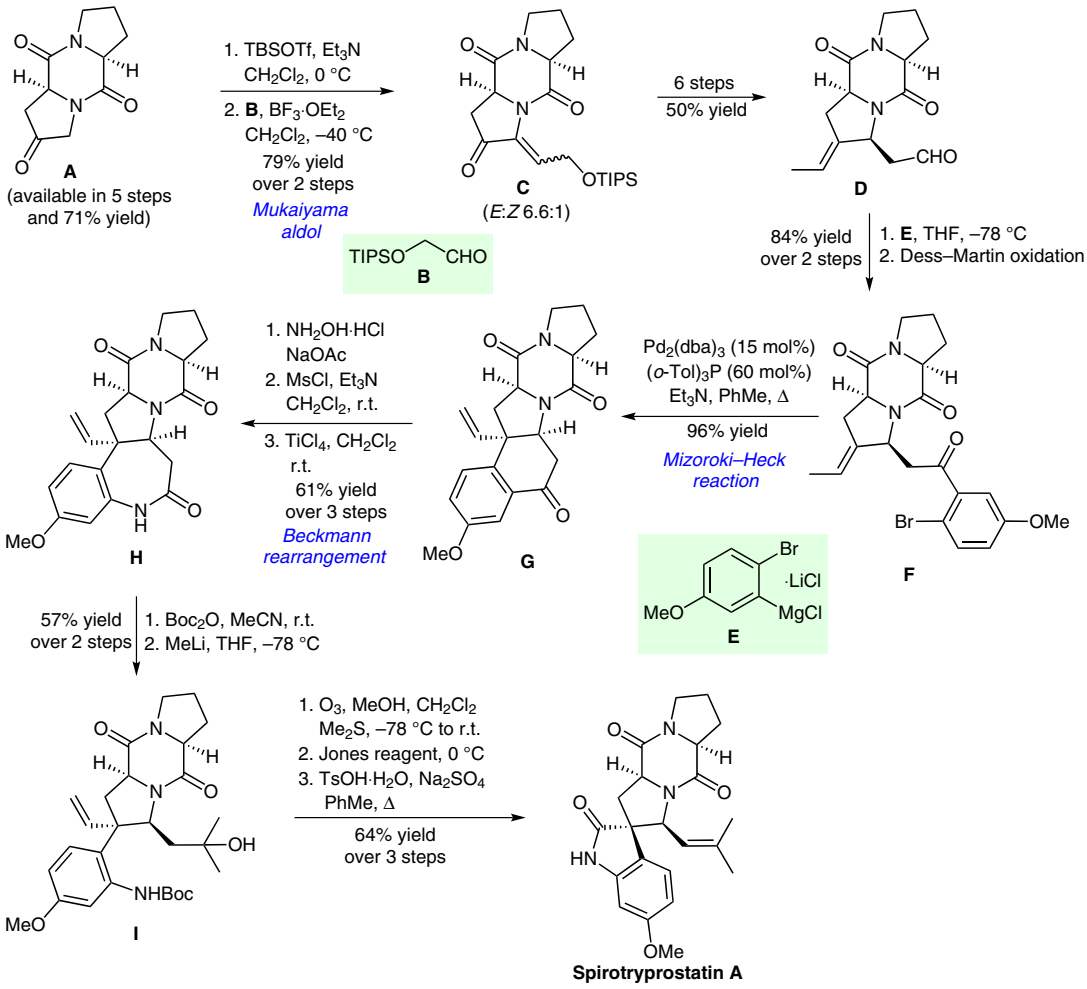
Total Synthesis of Spirotryprostatin A



Significance: Spirotryprostatin A, a spirocyclic diketopiperazine natural product that was isolated in 1996, was found to be an inhibitor of the mammalian cell cycle in G2/M phase and thus an interesting lead in drug discovery. A number of syntheses of spirotryprostatin A have been disclosed, and Fukuyama now describes a synthetic strategy that relies on a Heck reaction for the elegant installation of the quaternary stereocenter.

Comment: A silyl enol ether derived from diketopiperazine **A** underwent a Mukaiyama aldol reaction with aldehyde **B** to afford enone **C**, which was converted into aldehyde **D** in six steps. Addition of aryl Grignard **E** followed by oxidation of the resulting secondary alcohol furnished ketone **F**, which gave spirocycle **G** in the key Heck reaction. The anilide was then introduced through Beckmann rearrangement (**G** → **H**). **H** could be advanced into the target molecule in five additional steps.

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