Practical Asymmetric Synthesis of Efavirenz (DMP 266), an HIV-1 Reverse Transcriptase Inhibitor


Synthesis of Efavirenz via Asymmetric Alkynylation

**Significance:** Efavirenz (Sustiva®) is an HIV-1 reverse transcriptase inhibitor that was approved by the FDA in 1998 for the treatment of HIV/AIDS. The classic DuPont–Merck synthesis depicted incorporates a highly enantioselective addition of lithium acetylide $K$ (as the tetrameric complex $F$) to ketone $E$ mediated by chiral chaperone $J$. The synthesis proceeds in 62% overall yield in just seven steps. Since all intermediates were crystalline, no chromatography was required.


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Synfacts 2019, 15(01), 0005 Published online: 14.12.2018

DOI: 10.1055/s-0037-1611443; Reg-No.: K07318SF