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 (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.


Formation of the tetrameric complex \( F \):