Synthesis of Histone Acetyltransferase Inhibitor A-485

**Significance:** A-485 is a histone acetyltransferase (HAT) domain inhibitor. The key step in the synthesis depicted is the construction of the stereogenic center in G by catalytic asymmetric cyanosilylation. Intermediate G was initially obtained in only 77% ee. Enhancement of the ee required a combination of trituration, chromatography, and crystallization (2×) to give G in 59% yield (>99% ee) from D.

**Comment:** The asymmetric cyanosilylation entails a catalytic double-activation in which a chiral aluminium Lewis acid derived from B (2 mol%) activates the electrophile and an achiral Lewis base (N-oxide C, 1 mol%) activates the nucleophile (X. M. Feng et al. Chem. Eur. J. 2004, 10, 4790).