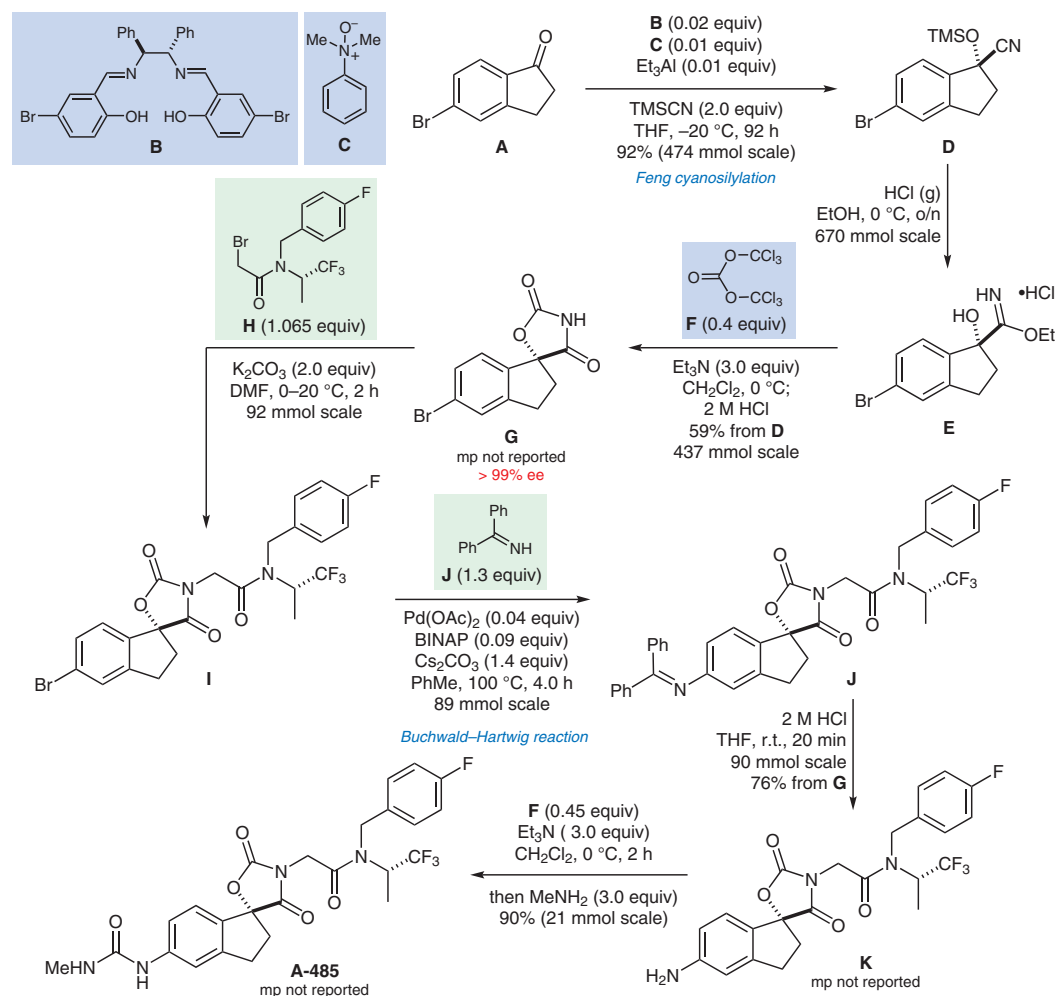


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 Discovery of Spiro Oxazolidinediones as Selective, Orally Bioavailable Inhibitors of p300/CBP Histone Acetyltransferases
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Synthesis of Histone Acetyltransferase Inhibitor A-485



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 \times) 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).

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