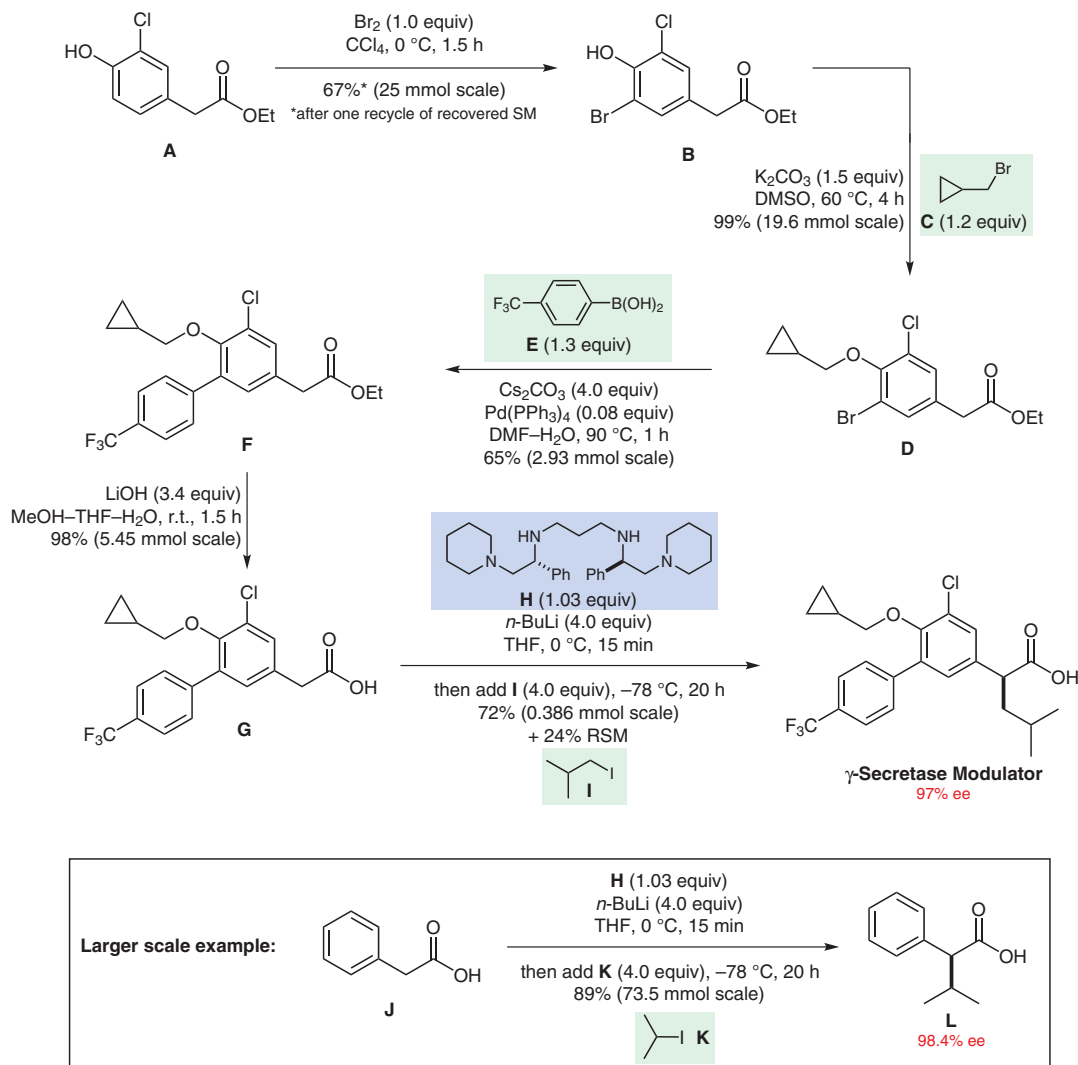


Synthesis of a γ -Secretase Modulator



Significance: The synthesis of the γ -secretase modulator depicted illustrates an efficient enantioselective alkylation of enediolates derived from arylacetic acids using the chiral lithium amide base **H** as a stereodirecting agent. The chiral base is required in stoichiometric amounts, but it is recoverable and easily prepared in two steps from styrene oxide (M. J. Frizzle et al. *Org. Process Res. Dev.* **2007**, *11*, 215).

Comment: The scope of the asymmetric alkylation was established using 24 aryl- and heteroarylacetic acids and 12 alkylating agents (36 examples in total) with yields typically exceeding 70% (6 exceptions) and ee values typically exceeding 90% (5 exceptions). Under the standard conditions outlined above, simple alkanolic acids did not undergo highly enantioselective alkylation.