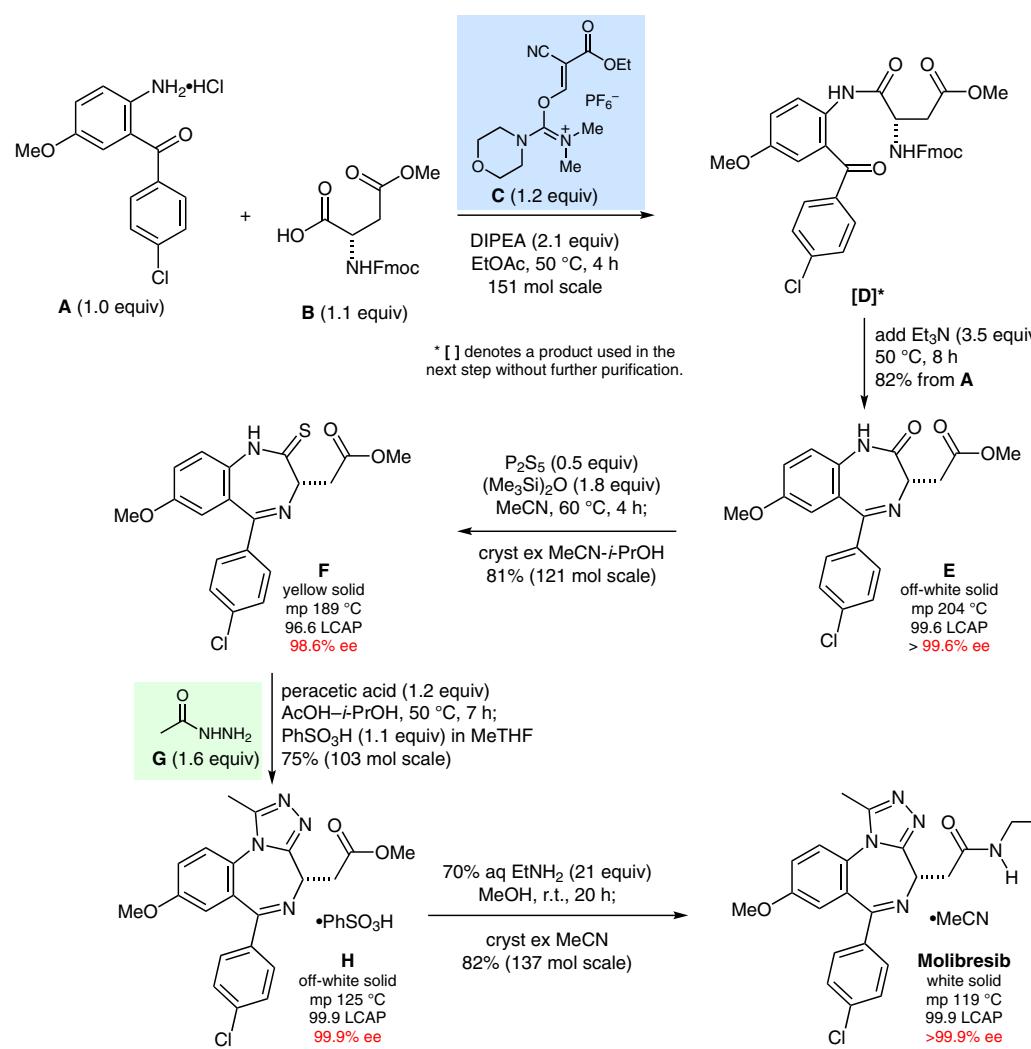


## Synthesis of Molibresib



**Significance:** Molibresib (GSK525762) is an inhibitor of the interaction between bromo and extra-terminal (BET) bromodomain proteins that is of interest for the treatment of solid tumors. The concise synthesis of molibresib depicted started with the commercially available ketone **A** and delivered 52 kg of product in 41% yield and 99.9% ee. For the discovery synthesis of molibresib, see: E. Nicodeme et al. *Nature* **2010**, *468*, 1119.

**Comment:** Construction of the core methyltriazolo[1,4]benzodiazepine **H** was achieved by oxidative activation of the thiolactam **F** via a sulfinic acid (RS-OH) that underwent substitution by acetylhydrazide (**G**), followed by an acid-catalyzed cyclization. The mild conditions for the methyltriazole formation avoided racemization of the sensitive stereocenter.