Category

Synthesis of Natural Products and Potential Drugs

Key words

BMS-986158

Stille coupling

Chan–Lam coupling

copper catalysis

palladium-catalyzed C–H activation

Mitsunobu reaction

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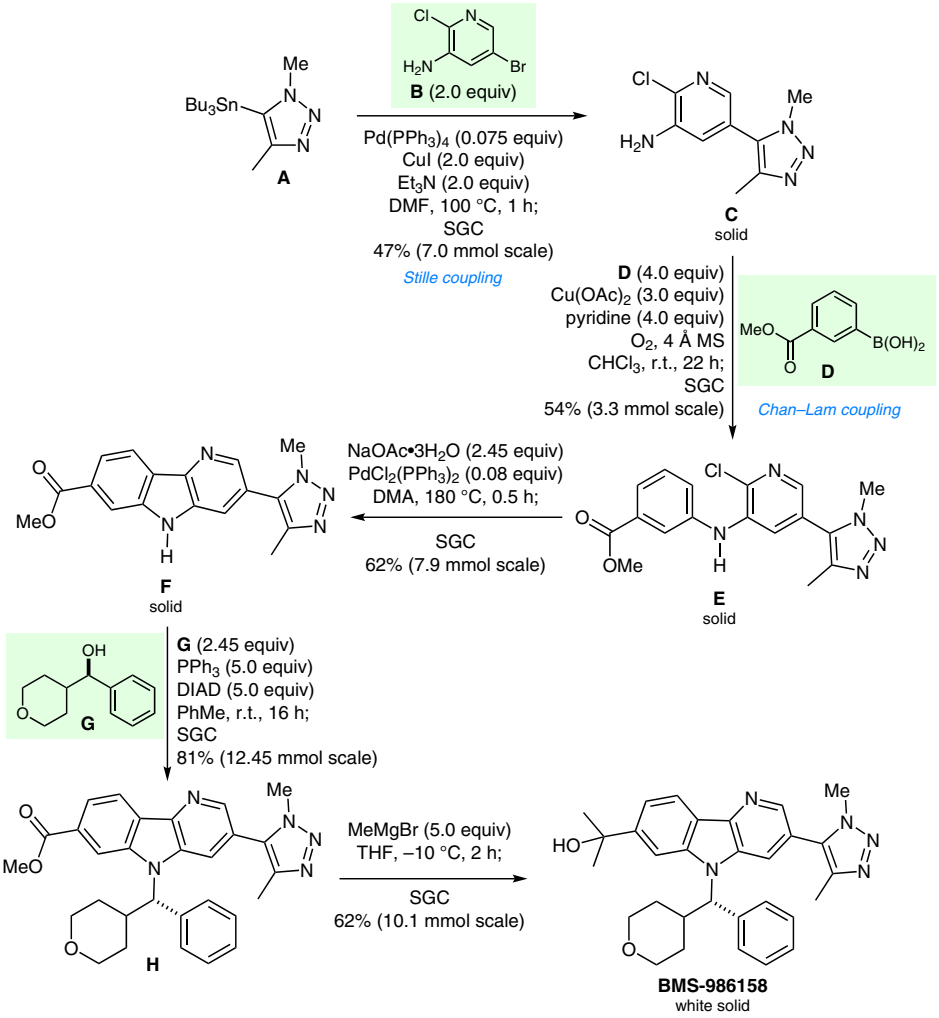
Discovery and Preclinical Pharmacology of an Oral Bromodomain and Extra-Terminal (BET) Inhibitor Using Scaffold-Hopping and Structure-Guided Drug Design

J. Med. Chem. **2021**, *64*, 14247–14265, DOI: 10.1021/acs.jmedchem.1c00625.

Synthesis of BMS-986158



Significance: BMS-986158 is an inhibitor of the bromodomain and extra-terminal (BET) family of adaptor proteins that are involved in the transcriptional regulation of key oncogenes. It has entered phase 1/2a clinical trials in patients with advanced cancers and hematologic indications including myelofibrosis.

Comment: Key steps in the small-scale discovery synthesis of the 5*H*-pyrido[3,2-*b*]indole core of BMS-986158 are (1) the copper-catalyzed oxidative coupling of the chloropyridine **C** with the boronic acid **D** (Chan–Lam coupling) and (2) the palladium-catalyzed C–H activation reaction **E** → **F**.

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Synfacts 2021, 17(12), 1314 Published online: 17.11.2021
DOI: 10.1055/s-0041-1737090; **Reg-No.:** K07021SF