M. D. EASTGATE* ET AL. (BRISTOL-MYERS SQUIBB, NEW BRUNSWICK, USA)
Ni-Catalyzed C–H Functionalization in the Formation of a Complex Heterocycle: Synthesis of the Potent JAK2 Inhibitor BMS-911543
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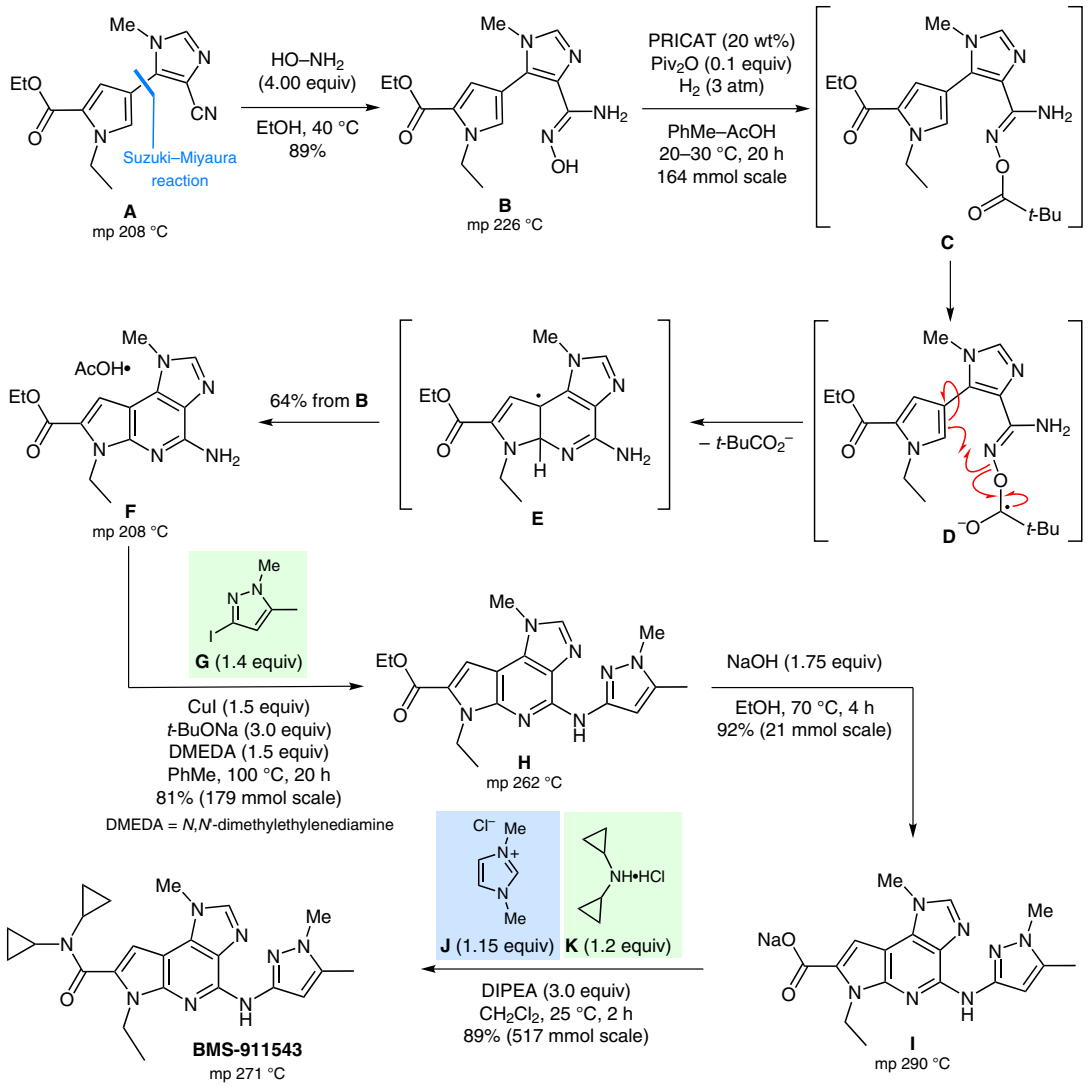
Synthesis of JAK2 Inhibitor BMS-911543



Significance: BMS-911543 is a selective JAK2 kinase inhibitor that is of interest for the treatment of myeloproliferative disorders. The key step in the synthesis depicted is the nickel-mediated cyclization (**B** → **F**) that enabled the construction of the highly functionalized 1*H*-pyrrolo[2,3-*b*]pyridine core in just eight steps (29% overall yield) from ethyl 4-bromo-1*H*-pyrrole-2-carboxylate.

Comment: The final amide bond formation was complex owing to the instability of dicyclopropylamine (DCPA). After screening a variety of more unusual conditions, 2-chloro-1,3-dimethylimidazolidinium chloride (**J**) cleanly and quantitatively formed the acid chloride of carboxylate **I** which smoothly coupled with DCPA.

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Category
Synthesis of Natural Products and Potential Drugs

Key words
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1*H*-pyrrolo[2,3-*b*]-pyridines
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