# Efficient Industrial Synthesis of Idasanutlin via a Cu(I)-catalyzed [3+2] Asymmetric Cycloaddition

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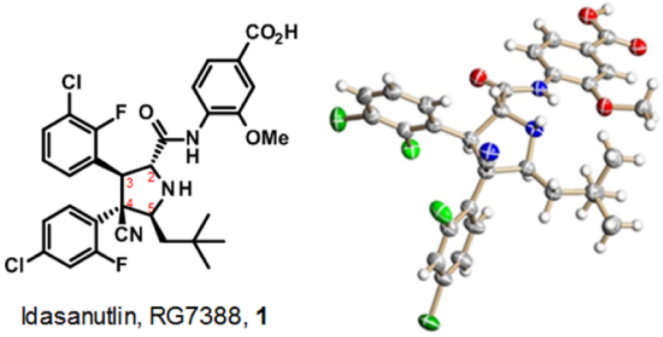
A concise asymmetric synthesis has been developed to prepare idasanutlin (1), a small molecule MDM2 antagonist currently being investigated as a potential treatment for various solid tumors and hematologic malignancies. The highly congested pyrrolidine core, containing four contiguous stereocenters, was constructed via a Cu(I)/BINAP catalyzed [3+2]-cycloaddition reaction. This optimized copper(I) catalyzed process has been used to produce more than 1500 kg of idasanutlin.




Idasanutlin, RG7388, **1**

The evolution of this synthetic route from the laboratory to commercial-scale manufacturing will be described, highlighting the exceptionally selective and consistent cycloaddition/isomerization/ hydrolysis sequence. The excellent yields, short cycle times and reduction in waste streams result in a sustainable production process with low environmental impact.

[1] Rimmler, G. Alker, A. Bosco, M. Diodone, R. Fishlock, D. Hildbrand, S. Kuhn, B. Moessner, C. Peters, C. Rege, P.D. Schantz, M. *Org. Process Res. Dev.* **2016**, *20*, 2057-2066.