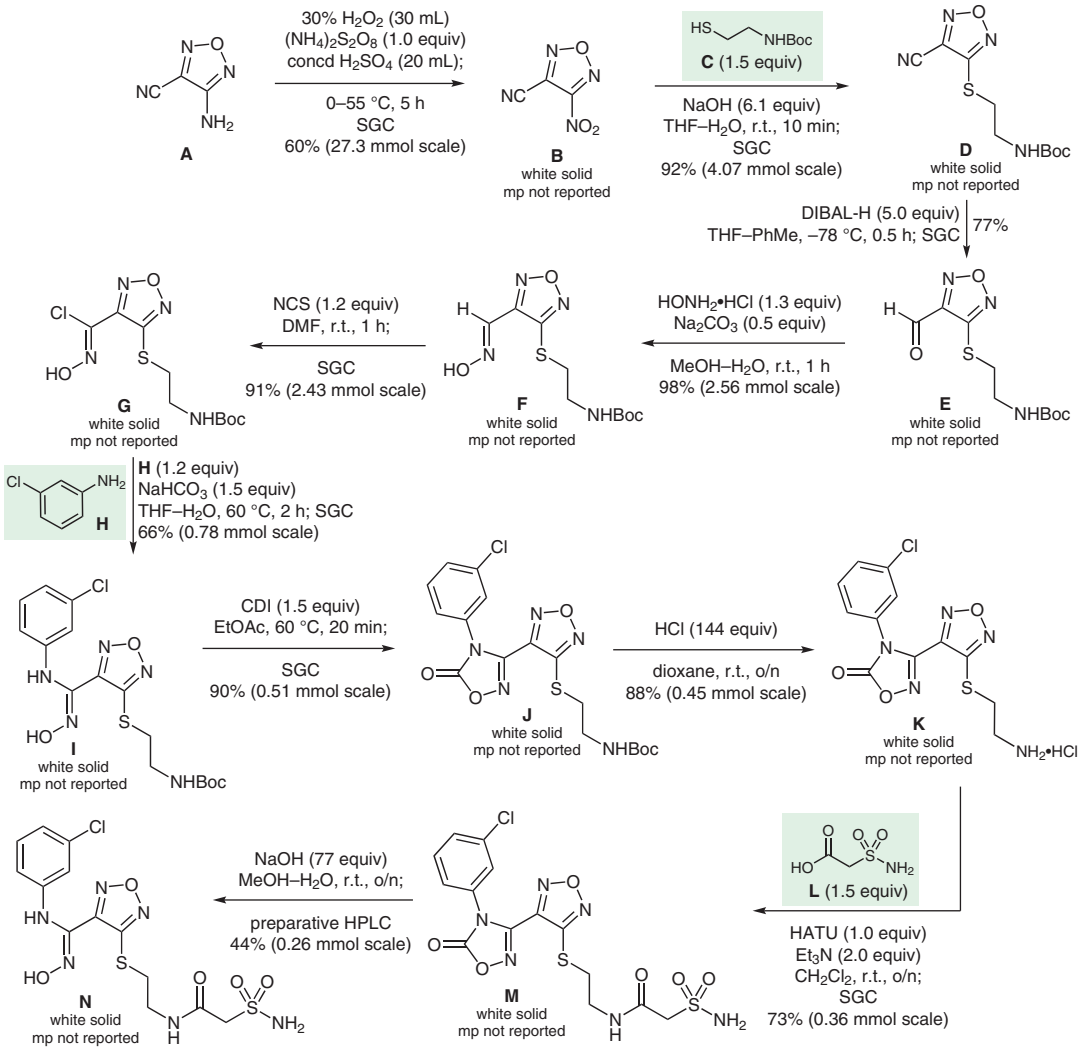
C. STEENECK*, O. KINZEL, S. ANDERHUB, M. HORNBERGER, S. PINTO, B. MORSCHHAEUSER, F. BRAUN, G. KLEYMANN, T. HOFFMANN (PHENEX PHARMACEUTICALS AG, HEIDELBERG, GERMANY)

Discovery of Hydroxyamidine Based Inhibitors of IDO1 for Cancer Immunotherapy with Reduced Potential for Glucuronidation
ACS Med. Chem. Lett. **2020**, *11*, 179–187.

Synthesis of an Indoleamine-2,3-dioxygenase-1 (IDO1) Inhibitor



Significance: Indoleamine-2,3-dioxygenase-1 (IDO1) is strongly involved in tumor immune resistance. The immune suppressive effect of IDO1 results from its capacity to degrade tryptophan to *N*-formylkyurenine, the first and rate-limiting step of the kyurenine pathway. The target molecule **N** is a low-nanomolar IDO1 inhibitor.

Comment: Reaction of aldoxime **F** with *N*-chlorosuccinimide (NCS) afforded *N*-hydroxycarbimidoyl chloride **G**. Treatment of **G** with 3-chloroaniline followed by hydroxyamidine cyclization using 1,1′-carbonyldiimidazole (CDI) and Boc deprotection afforded the key amino intermediate **K**.

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Category

Synthesis of Natural Products and Potential Drugs

Key words

indoleamine-2,3-dioxygenase-1 inhibitor

1,2,4-oxadiazole

S_NAr reaction

Synfact of the Month