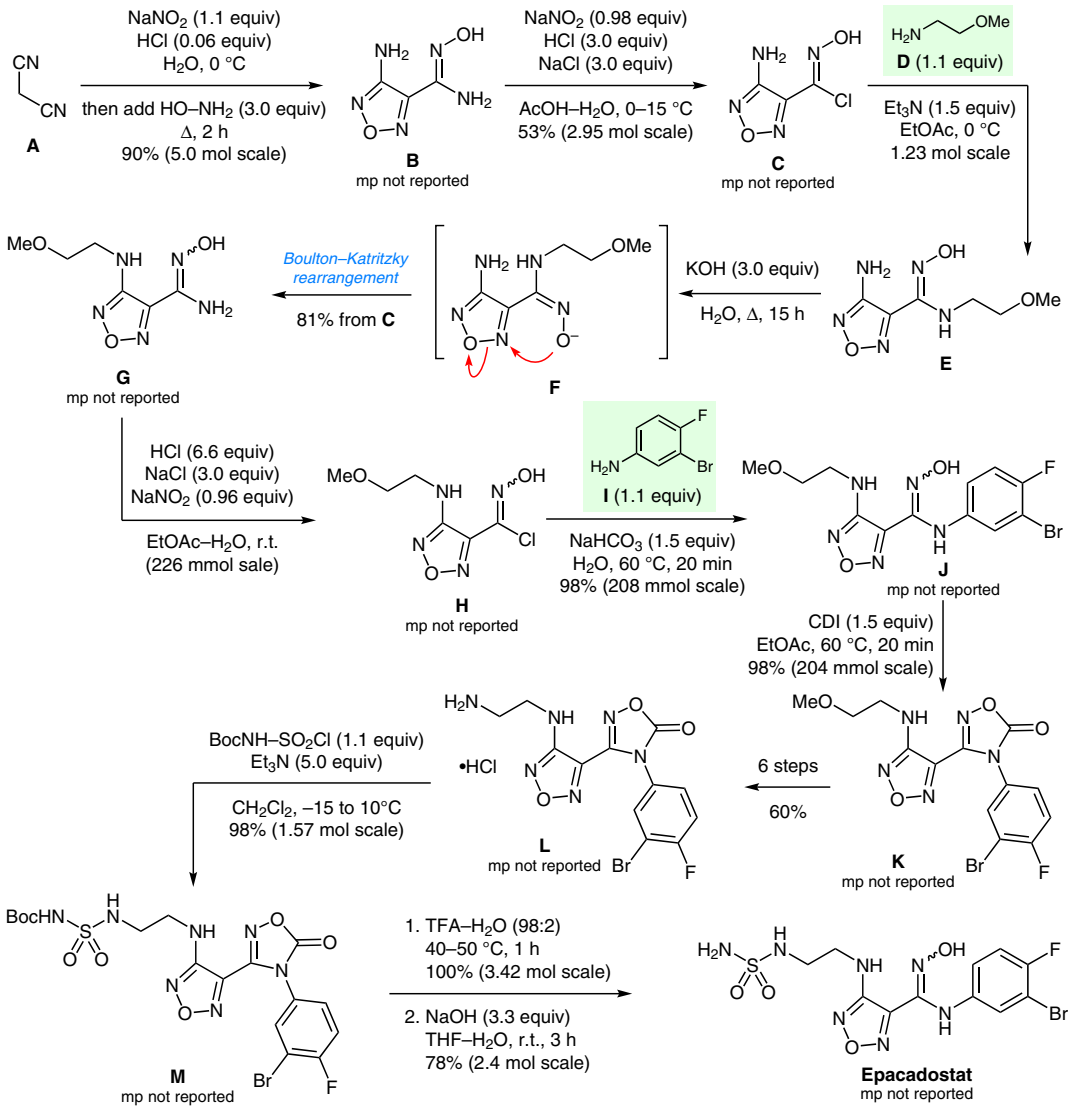
A. P. COOMBS* ET AL. (INCYTE CORPORATION, WILMINGTON, USA)

INCB24360 (Epacadostat), a Highly Potent and Selective Indoleamine-2,3-dioxygenase 1 (IDO1) Inhibitor for Immuno-oncology
ACS Med. Chem. Lett. **2017**, *8*, 486–491.

Synthesis of Epacadostat



Significance: Epacadostat (INCB24360) inhibits the immunomodulatory activity of indoleamine-2,3-dioxygenase 1, thereby making possible the restoration and/or activation of the immune system in cancer therapy. In combination with pembrolizumab, epacadostat is currently in a phase III clinical trial for the treatment of metastatic melanoma.

Comment: Synthesis of the secondary 3-amino-furazan **G** by direct alkylation or reductive amination of the primary 3-amino substituent in **E** was low yielding, presumably due to the electron deficiency of the furazan. A general and robust alternate route to secondary amino-furazan **G** was accomplished through a Boulton–Katritzky rearrangement of the amidooxime furazan **E**.

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Category

Synthesis of Natural Products and Potential Drugs

Key words

epacadostat

indoleamine-2,3-dioxygenase 1 inhibitors

furazan ring formation

Boulton–Katritzky rearrangement

hydroxyamidines