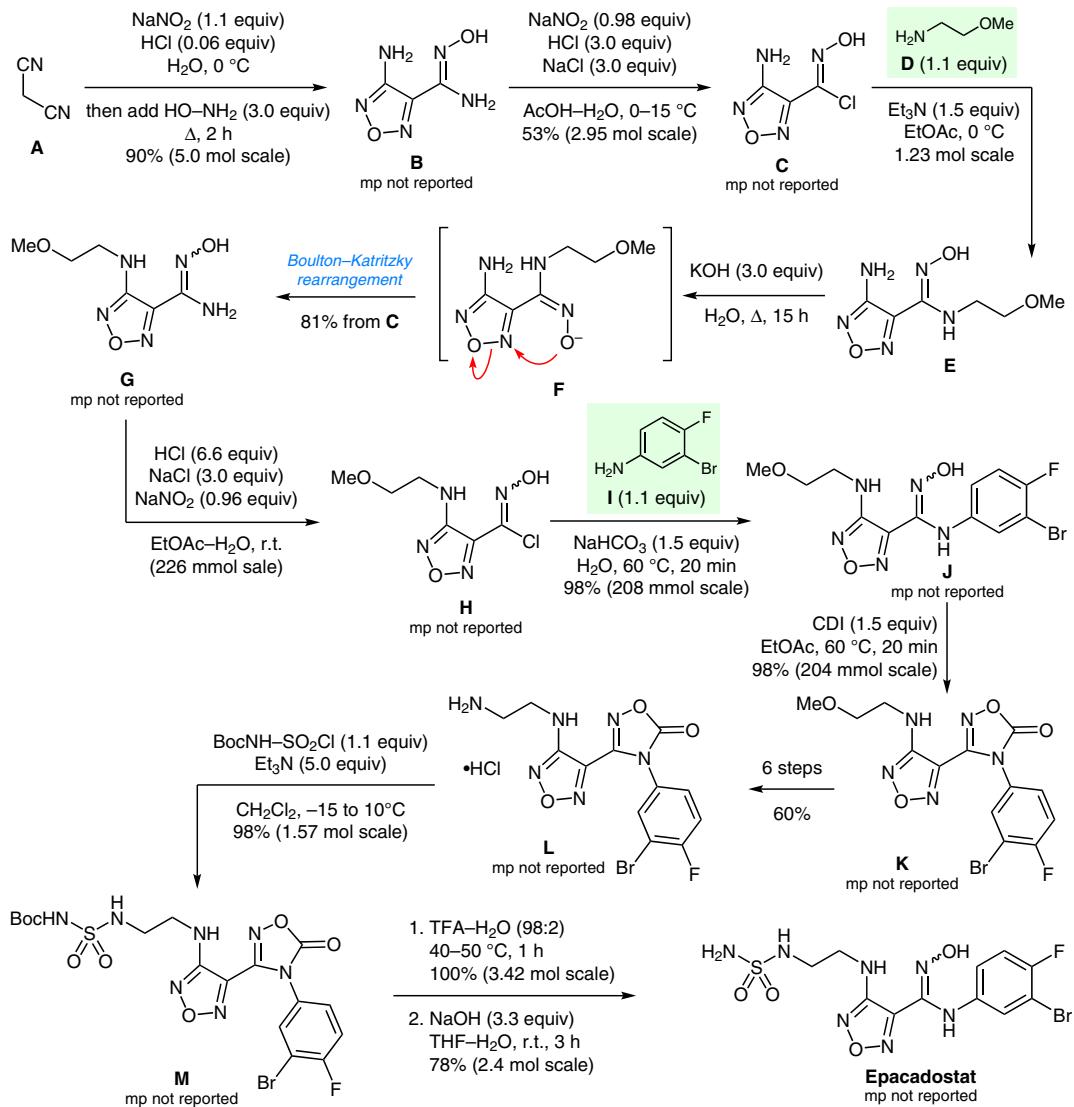


Synthesis of Epacadostat



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.

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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.

Key words

- epacadostat
- indoleamine-2,3-dioxygenase 1 inhibitors
- furazan ring formation
- Boulton-Katritzky rearrangement
- hydroxyamidines

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of the month