An Efficient Process for the Manufacture of Carmegliptin


## Synthesis of Carmegliptin

### Significance:
Carmegliptin is a dipeptidyl dipeptidase-IV inhibitor under development for the treatment of type-2 diabetes. Over 1000 kg was synthesized by the route depicted featuring an efficient crystallization-induced dynamic resolution of rac-D and a large-scale Hofmann rearrangement of the amide F.

### Comment:
J.-M. Adam et al. (Org. Process Res. Dev. 2011, 15, 515) describe the synthesis of lactone H by asymmetric hydrogenation (10 kg scale), but a route starting from commercial (S)-tert-butyl glycidyl ether (derived from a Jacobsen hydrolytic kinetic resolution) delivered >500 kg of H.

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