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Catalytic Enantioselective Allylic Amination of Olefins for the Synthesis of *ent*-Sitagliptin
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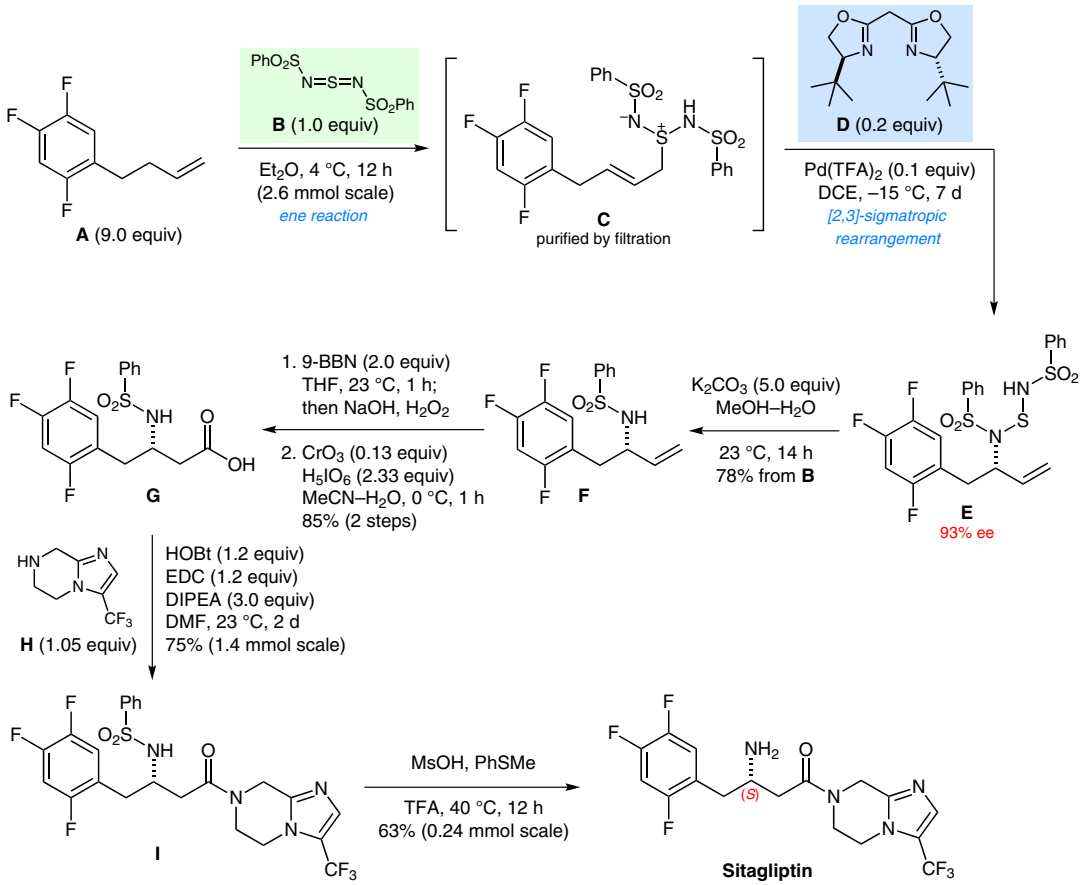
Synthesis of (*S*)-Sitagliptin



Significance: Sitagliptin is a dipeptidyl dipeptidase-4 inhibitor that is prescribed for the treatment of type II diabetes. The small-scale synthesis depicted features a two-step construction of the allylic amine **E** involving an ene reaction using the sulfurdiimide **B** followed by a palladium-catalyzed asymmetric [2,3]-sigmatropic rearrangement of ylid **C**.

Comment: The ylid **C** does not undergo a [2,3]-sigmatropic rearrangement at 4 °C in the absence of the palladium catalyst. A further five 4-arylbut-1-ene substrates with F, CF_3 and OMe substituents gave the allylic amination products in 79–94% yield and 81–94% ee.

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Category

Synthesis of Natural Products and Potential Drugs

Key words

sitagliptin

dipeptidyl dipeptidase-4 inhibitor

asymmetric allylic amination

palladium

ene reaction

[2,3]-sigmatropic rearrangement