**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 involving an ene reaction using the sulfurdiimide followed by a palladium-catalyzed asymmetric [2,3]-sigmatropic rearrangement of ylid. 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, CF₃ and OMe substituents gave the allylic amination products in 79–94% yield and 81–94% ee.

**Comment:**

- **(S)-Sitagliptin**

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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