

Enantioselective Synthesis of Sphingadienines and Aromatic Ceramide Analogs[‡]

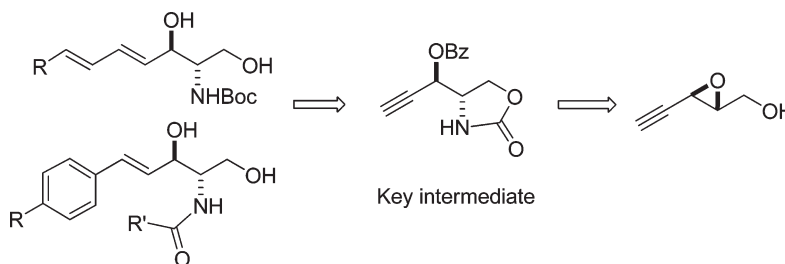
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ABSTRACT



A new approach to the synthesis of sphingoid bases has been developed. The strategy is based on Sonogashira coupling of a chiral acetylenic carbamate that can be prepared in enantiomerically enriched form from 2,3-epoxy-4-pentyn-1-ol, which is readily accessible by Sharpless asymmetric epoxidation. Several *N*-Boc-sphingadienines and aromatic ceramide analogs have been synthesized.

Glycosphingolipids are constituents of eukaryotic cell membranes¹ and play important roles in many physiological processes.² The basic components of these lipids are called *sphingosines* and have a characteristic 2-amino-1,3-diol fragment with a 2*S*,3*R* (*D*-erythro) configuration³ (Figure 1). Ceramides are fatty acid sphingosine amides and have been implicated in the regulation of cell growth and differentiation, inflammation, and apoptosis.⁴ Ceramides have been implicated in many physiological events.⁵ The C(4)–C(5) *trans* double bond in the sphingoid base

may be crucial for the biological activities of ceramides. Sphingosines are potent inhibitors of protein Kinase C.⁶ There is growing interest in the development of sphingosine analogs. For instance, sphingosines with aromatic substituents in the side chain⁷ are stronger sphingosine kinase inhibitors relative to their corresponding parent compounds.⁸ Sphingadienines, which have two double bonds in the hydrocarbon chain, are less abundant sphingoid bases.⁹ Over the past few years, ceramide analogs with

[‡] Dedicated to Prof. Rafael Suau (Universidad de Málaga), in memoriam.

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