Enantioselective Synthesis of the Quinone Epoxide Dimer (+)-Torreyanic Acid.

Torreyanic acid (1, Figure 1), a dimeric epoxyquinoid natural product, was isolated and structurally characterized by Lee and co-workers in 1996. A biosynthetic scheme for the synthesis of the natural product was proposed involving Diels-Alder dimerization of diastereomeric 2H-pyran monomers. Recently, the first total synthesis and absolute stereochemical assignment of the quinone epoxide dimer (+)-torreyanic acid has been accomplished employing a [4+2] dimerization of diastereomeric 2H-pyran monomers.

Figure 1. Retrosynthetic analysis.

Synthesis of the related monomeric natural product (+)-ambuic acid (2, Figure 2) has also been achieved which establishes the biosynthetic relationship between these two natural products. A tartrate-mediated nucleophilic epoxidation involving hydroxyl group direction facilitated the asymmetric synthesis of the key chiral quinone monoepoxide intermediate. Thermolysis experiments have also been conducted on a model dimer based on the torreyanic acid core structure and facile retro Diels-Alder reaction processes and equilibration of diastereomeric 2H-pyran monomers have been observed. Higher temperature thermolysis of the model dimer led to the production of a novel monomeric compound by an apparent pericyclic cascade involving retro [4+2], electrocyclic ring-opening, 1,7-hydride shift, and final disrotatory 6π electrocyclization. In addition, theoretical calculations of Diels-Alder transition states have been performed to evaluate alternative transition states for Diels-Alder dimerization of 2H-pyran quinone epoxide monomers and provide insight into the stereocontrol elements for these reactions. J. Am. Chem. Soc. 2003, 125, 5095-5106

Figure 2: Syntheses of (+)-torreyanic acid and (+)-ambuic acid from common intermediate indicating possible biosynthetic relationship of these two natural products.