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Total Synthesis of a Library of Unnatural Derivatives of Lingzhiol

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Lingzhiol, a tetracyclic meroterpenoid, has an unprecedented structure and exhibits selective inhibitory activity toward p-Smad proteins, which is relevant to the treatment and prevention of renal fibrosis, a common and often fatal final pathway of chronic kidney disease. Discovered by Cheng and colleagues, lingzhiol was isolated in minute quantities from *Ganoderma lucidum*, a tropical fungus commonly used in traditional Chinese medicine under the name ling-zhi (靈芝). Dr. Vladimir Birman and Krishna Sharma Gautam have recently published a novel 9-step synthesis of lingzhiol, which utilizes an acid-catalyzed semipinacol rearrangement of a glycidyl alcohol intermediate. Using variations on this flexible scheme, a library of unnatural lingzhiol derivatives are being synthesized, with particular focus on altering the substitution pattern on the benzene ring. These derivatives will be sent to the Washington University School of Medicine for further investigation of their antifibrotic and neurotrophic activities.