

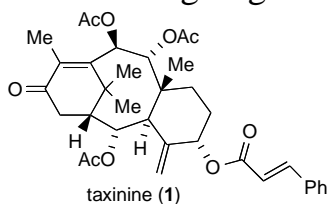
Recent Progress in the Chemical Synthesis of Taxinine and Other Cyclooctanoid Natural Products

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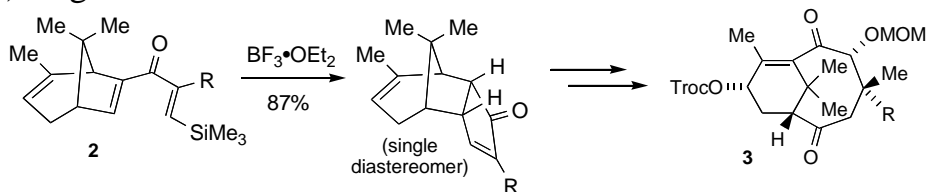
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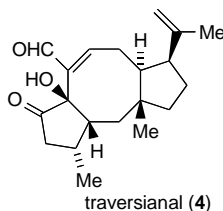
Taxinine (**1**) and related naturally occurring taxanes have shown promise as potential multidrug resistance (MDR) reversal agents. With an eventual goal of developing new drug leads based on a simplified taxoid framework, we have embarked upon the chemical synthesis of this interesting target compound.



Utilizing a highly diastereoselective Nazarov cyclization¹ of bridged bicyclic dienone **2**, a series of tricyclic products has been prepared, in which the diquinane structure present in the tricyclic skeleton serves as a hidden 8-membered B-ring. Subsequent introduction of a ring-fusing alkene followed by oxidative cleavage then reveals the taxane AB system (**3**). Current work is focusing on the elaboration of the remaining (C) ring.



We also have a longstanding interest in the chemical synthesis of various members of the fusicoccin class of diterpenes, possessing a challenging 5-8-5 tricyclic skeleton. Initial efforts are focused on the antifungal natural product, traversianal (**4**). We are approaching this objective using a novel and stereoselective [4+4]-photocycloaddition process involving pyran-2-ones.²



Recent progress in these synthetic studies will be discussed, along with some digressions involving the key methodologies used to assemble the core skeletons.

¹ (a) Mazzola, R. D., Jr.; White, T. D.; Vollmer-Snarr, H. R.; West, F. G. *Org. Lett.* **2005**, *7*, 2799–2801. (b) Giese, S.; Mazzola, R. D., Jr.; Amann, C. M.; Arif, A. M.; West, F. G. *Angew. Chem. Int. Ed.* **2005**, *44*, 6546–6549.

² Song, D.; McDonald, R.; West, F. G. *Org. Lett.* **2006**, *8*, 4075–4078.