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DESIGN AND SYNTHESIS OF SIMPLIFIED PACLITAXEL ANALOGS BASED ON THE T-TAXOL BIOACTIVE CONFORMATION

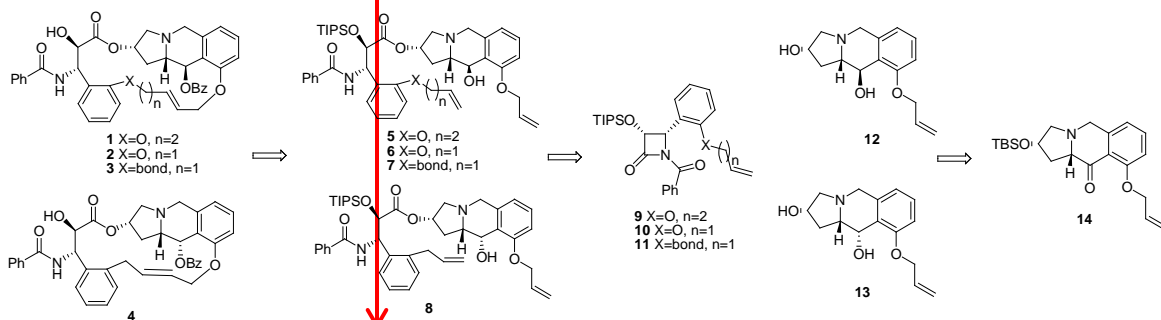
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Jielu Zhao¹, Susan Bane², James P. Snyder³, Haipeng Hu³, Kamalika Mukherjee², and David G. I. Kingston¹. ¹Department of Chemistry, Virginia Polytechnic Institute & State University, Blacksburg, VA 24061, USA, ²Department of Chemistry, Binghamton University, Binghamton, NY 13902, ³Department of Chemistry, Emory University, 1515 Dickey Drive, Atlanta, GA 30322

The simplified paclitaxel analogs **1-4** have been designed as compounds which should bind to tubulin, based on their similarity to the T-taxol conformation. One caveat is their increased flexibility relative to paclitaxel. The target compounds were synthesized by Grubbs' metatheses of compounds **5-8**, which were prepared by coupling β -lactams **9-11** with alcohols **12** and **13**. Compounds **12** and **13** were formed by reduction of the intermediate **14**, which was constructed by coupling a *cis*-4-hydroxyproline derivative with 3-(allyloxy)-2-iodobenzaldehyde. The syntheses of **1-4** together with their biological data will be presented.

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