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

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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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