Mechanistic Possibilities for Oxetane Formation in the Biosynthesis of Taxol's D Ring

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Abstract—Three mechanistic possibilities for the formation of the oxetane (D ring) of Taxol were examined at various levels of theory [B3LYP/6-31+G(d,p), mPW1PW91/6-31+G(d,p), and MP2/6-31+G(d,p)] including one mechanism involving an unusual oxabicyclobutonium ion intermediate. The mechanisms examined differ considerably in terms of their predicted inherent activation barriers, and the requirements for acceleration of each by an enzyme active site are outlined. Our calculations provide an important starting point for future studies in this area. Also examined were previously published calculations on simple oxabicyclobutonium ions, as well as the all-carbon analog of the pathway involving the oxabicyclobutonium ion.

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