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Synthesis of C-5 and C-10 Vinyloxybenzene Containing Substrates for the Enzyme Protein Farnesyltransferase

Abstract

Protein Farnesyltransferase (PFTase) is an enzyme that incorporates farnesyl groups into proteins and peptides that end in a certain amino acid sequence. Previously, non-natural substrates that could have also been transferred by PFTase have undergone bioconjugation reactions via copper catalyzed click chemistry. Because of copper’s cytotoxicity, these substrates are not compatible with in vivo applications.

Presented are two bioorthogonal substrates that do not require the use of a copper catalyst and they contain a vinyloxybenzene moiety for a photoreaction on a diaryl tetrazole. Both substrates are predicted to be PFTase substrates that will allow for the eventual incorporation of new properties such as fluorescence on targeted proteins. Because many prenylated proteins are involved in signaling processes, this has generated interest in protein prenyl transferases as possible anticancer targets.