Exploring Redox Mediated Triggering Mechanisms to Promote Bergman Cyclization of Metalloenediynes

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Many natural product-containing enediynes which have shown activity as antitumor agents possess triggering functionalities that when activated promote thermally induced Bergman cyclization. In the presence of DNA, the diradical intermediate performs H-atom abstraction from the phosphodiester backbone leading to DNA cleavage and apoptosis. Geometric control of Bergman cyclization has been realized through coordination of an enediyne ligand to a metal center which reduces the interalkynyl distance and subsequently the cyclization barrier. Using the ligand 1,2-bis((diphenylphosphino)ethynyl)benzene, a Pt(0) complex has been synthesized and characterized. This d¹⁰-tetrahedral complex shows only modest reduction of the alkyne termini separation and Bergman cyclization temperature. Oxidation of this reduced species to the Pt(II) d⁸ analog may serve as a potential triggering mechanism for geometric rearrangement to square planar geometry resulting in a decreased interalkynyl distance and cyclization temperature. Preliminary results in this theme will be discussed.