Possible Tautomeric Triggers of the Bergman Cyclization of Enediynes

Arjun Jaini and Carol A. Parish
Department of Chemistry, University of Richmond, VA

Enediynes have potential as anti-cancer pro-drugs. Enediynes cyclize via the well-studied Bergman Cyclization to form para-benzyne. Para-benzyne is a diradical which destroys cancer cells by extracting hydrogen atoms from tumor cell DNA. Although this reaction can be initiated with light or heat, an efficient way to trigger the Bergman cyclization only in the presence of a cancer cell has yet to be found. Keto-enol tautomerization was studied as a possible trigger for the Bergman Cyclization of enediynes. The activation barriers and reaction energies for the cyclization of 3,4-diethynylpridin-2-ol and 3, 4-diethynylpyridin-2(1H)-one were calculated and compared using density functional theory with a 6-31G** basis set and a UB3LYP functional. The difference between the activation energies of these two molecules at this level of theory was less than 1 kcal/mol, suggesting that both tautomeric forms of the structure have a similar effect on the Bergman cyclization.