Density Functional Study of Asymmetric N-Heterocyclic Carbene (NHC) Catalyzed Crossed Aldehyde-Ketone Benzoin Cyclizations

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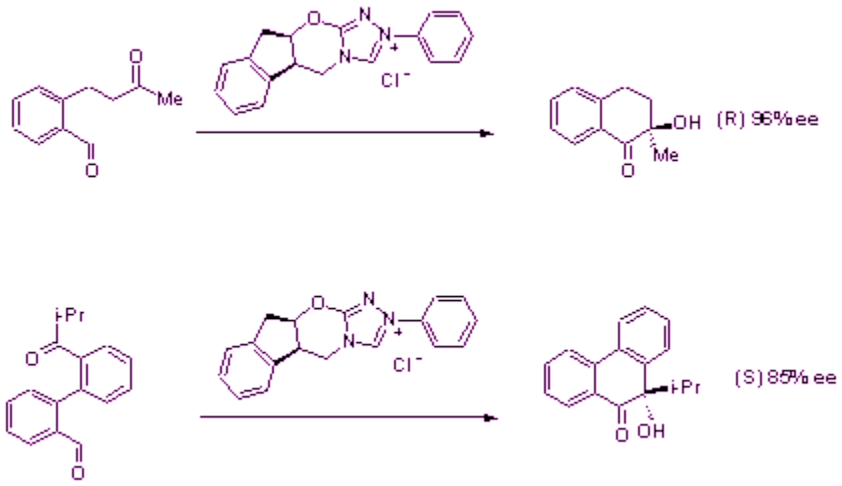
Density functional theory was used to analyze enantioselectivities in N-heterocyclic carbene catalyzed crossed aldehyde-ketone benzoin cyclizations recently reported by Suzuki et al [(1)]. A series of extensive transition state searches revealed that the reactions proceed via one of two routes: (1) a concerted process resembling the mechanism proposed by Dudding and Houk for triazolium/thiazolium catalyzed benzoin condensations; (2) a stepwise mechanism in which carbon-carbon bond formation followed by proton transfer occurs. In depth analysis of the transition states revealed that π- π stacking and hydrogen bonding play important roles in stabilization. The calculated models correctly predicted the sense of stereoinduction observed experimentally. Future work examining the inclusion of implicit solvation models is described.



(1) Takikawa, H.; Hachisu, Y.; Bode, J. W.; Suzuki, K. *Angew. Chem. Int. Ed.* **2006,** *45,* 3492-3494.