A Detailed Computational Investigation into Copper Catalyzed Sonogashira Coupling Reaction

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Abstract : Sonogashira coupling reactions are widely employed in the synthesis of molecules of biological and pharmaceutical importance. Copper catalyzed Sonogashira coupling reactions are gaining importance owing to the low cost and less toxicity of copper as compared to the palladium catalyst. In the present work, a detailed computational study has been carried out on the Sonogashira coupling reaction between aryl halides and terminal alkynes catalyzed by Copper (I) species with trans-1, 2 Diaminocyclohexane as ligand. All calculations are performed at Density Functional Theory (DFT) level, using the hybrid Becke3LYP functional. Cu and I atoms are described using an effective core potential (LANL2DZ) for the inner electrons and its associated double-ζ basis set for the outer electrons. For all other atoms, 6-311G+* basis set is used. We have identified that the active catalyst species is a neutral 3-coordinate trans-1,2 diaminocyclohexane ligated Cu (I) alkyne complex and found that the oxidative addition and reductive elimination occurs in a single step proceeding through one transition state. This is owing to the ease of reductive elimination involving coupling of Csp2-Csp carbon atoms and the less stable Cu (III) intermediate. This shows the mechanism of copper catalyzed Sonogashira coupling reactions are quite different from those catalyzed by palladium. To gain further insights into the mechanism, substrates containing various functional groups are considered in our study to traverse their effect on the feasibility of the reaction. We have also explored the effect of ligand on the catalytic cycle of the coupling reaction. The theoretical results obtained are in good agreement with the experimental observation. This shows the relevance of a combined theoretical and experimental approach for rationally improving the cross-coupling reaction mechanisms.

Keywords : copper catalysed, density functional theory, reaction mechanism, Sonogashira coupling
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