

Synthesis, Characterization, and Quantum Investigations on [3+2] Cycloaddition Reaction of Nitrile Oxide with 1,5-Benzodiazepine

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Abstract : Due to (3 + 2) cycloaddition and condensation reaction, a wide range of synthetic routes can be used to obtain biologically active heterocyclic compounds. Condensation and (3+2) cycloaddition reactions in heterocyclic syntheses are versatile due to the wide variety of possible combinations of several atoms of the reactants. In this article, we first outline the synthesis of benzodiazepine 4 with two dipolarophilic centers (C=C and C=N) by condensation reaction. Then, we use it for cycloaddition reactions (3+2) with nitrile oxides to prepare oxadiazole-benzodiazepines and pyrazole-benzodiazepine compounds. ¹H and ¹³C NMR are used to establish all the structures of the synthesized products. These condensation and cycloaddition reactions were then analyzed using density functional theory (DFT) calculations at the B3LYP/6-311G(d,p) theoretical level. In this study, the mechanism of the one-step cycloaddition reaction was investigated. Molecular electrostatic potential (MEP) was used to identify the electrophilic and nucleophilic attack sites of the molecules studied. Additionally, Fukui investigations (electrophilic f⁻ and nucleophilic f⁺) in the various reaction centers of the reactants demonstrate that, whether in the condensation reaction or cycloaddition, the reaction proceeds through the atomic centers with the most important Fukui functions, which is in full agreement with experimental observations. In the condensation reaction, thermodynamic control of regio, chemo, and stereoselectivity is observed, while those of cycloaddition are subject to kinetic control.

Keywords : cycloaddition reaction, regioselectivity, mechanism reaction, NMR analysis

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