Mechanistic perspectives on piperidine-catalyzed synthesis of 1,5-benzodiazepin-2-ones

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Abstract:

This work introduced new members to the pharmaceutical family of 1,5-benzodiazepin-2-ones, 2a–e. These compounds were synthesized in moderate yields via the reaction of 1,2-bifunctional substrates (α-cyanocinnamates) with o-phenylenediamine in xylene. The conduction of the above reaction in the presence of piperidine has produced amazing product, N-alkenylimidazolone derivative (5), in addition to the traditional one, 1,5-benzodiazepin-2-one (2a) in 3:1 ratio. The density functional theory (DFT) could successfully explain the role of piperidine as an organic catalyst to produce both products in this ratio through ethanol-assisted mechanisms. It is also amazing that we could obtain 5 solely by the dry fusion of 2a through the thermal contraction of diazepinone ring into imidazolone one. The mechanism of diazepinone-imidazolone transformation was proposed and validated by the DFT calculations. The findings showed that the precise proton transfer of primary amino hydrogen of 2a is the play-maker in the reaction game. The proposed mechanisms of the three transformations can be useful for investigation of the formation and deformation of other 1,5-diazepine systems.

Keywords:

1,5-Benzodiazepin-2-one, Organocatalyst, Ethanol-assisted mechanism, Density functional calculations

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