World Academy of Science, Engineering and Technology
International Journal of Chemical and Molecular Engineering
Vol:19, No:04, 2025

Synthesis, Characterization of Benzodiazepine Derivatives through Condensation Reaction, Crystal Structure, and DFT Calculations

Authors : Samir Hmaimou, Marouane Ait Lahcen, Mohamed Adardour, Mohamed Maatallah, Abdesselam Baouid

Abstract : The stereoisomers (E)-2,2-dimethyl-4-(4-subsitutedstyryl)-2,3-dihydro-1H-[1,5]-benzodiazepine 3(a-d) were synthesized via the condensation reaction of 2,2,3 4-trimethyl-2,3-dihydro-1H-1,5-benzodiazepine (BZD) 1 with the benzaldehyde derivatives 2(a-d) in polar protic solvent as ethanol. The chemical structure of the prepared products was confirmed by NMR (^{1}H and ^{13}C), HRMS, and X-ray analysis of the crystal structure 3d. The condensation reaction was examined using DFT calculations at the theoretical level of B3LYP/6-311G(d,p). Frontier molecular orbital analysis shows that the most favorable interaction is between the HOMO of BZD 1 and the LUMO of 2(a-d). On the other hand, the calculation of the global reactivity indices (softness, hardness, and chemical potential) confirmed that benzodiazepine BDZ 1 act as a nucleophile, whereas the aldehyde derivatives 2(a-d) play the role of electrophile. Furthermore, we identified each reagent's reactive sites by the measurement of the reactivity indices to explain the experimentally observed regioselectivity, using Fukui local reactivity descriptors. A one-step mechanism reaction and order 2 water elimination were investigated. We also looked at how the electron-withdrawing groups (EWG) of various aldehydes affected the reaction's mechanism and the stability of products 3(a-d).

Keywords : benzodiazepine, DFT calculations, crystal structure, regioselective, condensation Reaction
Conference Title : ICSOCMC 2025 : International Conference on Synthetic Organic Chemistry and Medicinal Chemistry
Conference Location : New York, United States
Conference Dates : April 17-18, 2025