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Modeling Ring-chain-ring Tautomerization of N-(o-aryl)-4-Hydroxy-2-oxazolidinone Derivatives

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Oxazolidine ring involving compounds have been introduced as drugs for the treatment of insuline resistance, hyperglycemia and some lipid disorders.[1] Oxazolidine derivatives are heterocyclic compounds having axis of chirality enabling the formation of atropisomers via hindered rotation around the C_{aryl}-N_{sp2} bond. Dogan et al. have shown that there is a linear relationship between the experimentally determined enantiomerization barriers for N-(o-aryl)-2,4-oxazolidinediones and the van der Waals radii of the ortho halogen substitutents.[2] However the axially chiral N-(o-aryl)-4-hydroxy-2-oxazolidinone derivatives which derive from the diastereoselective reduction of N-(o-aryl)-2,4-oxazolidinediones do not show such a linear relationship.[3] This was taken as a proof for the existence of a different mechanism for the enantiomerization of these compounds. Hence, Dogan et al. have investigated the interconversion of enantiomers of N-(o-aryl)-4-hydroxy-2-oxazolidinone derivatives and the substituent effect on the enantiomerization barriers by focusing on a ring-chain-ring tautomerization mechanism for racemization.

Herein, a theoretical investigation on the ring chain tautomerization mechanism in oxazolidione derivatives has been carried out by using Density Functional Theory (DFT). The solvent effect is also included both explicitly and implicitly. It has been found that there are two possible ring-chain-ring tautomerization pathways involving two different intermediates. All geometry optimizations have been performed at the B3LYP/6-31+G(d,p) level. Single point energy calculations have been also carried out for all structures at the BMK, MPWB1K and MP2 levels using the 6-31+G(d,p) basis set.

[1] Fujita, T.; Fujimoto, K.; Yoshioka, T.; *US Patent* **1996**.
[2] Demir Ordu, Ö.; Doğan, İ.; *Tetrahedron: Asymmetry* **2004**, 925–933.
[3] Demir Ordu, Ö.; Doğan, İ.; *Chirality* **2010**, 641-654.