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Substitution Group Effect on the Inhibition of Ubiquitin C-Terminal Hydrolases for Parkinson's Disease Study: Synthesis and Computational Analysis

Parkinson's disease is a neurodegenerative disorder that deteriorates motor function which can result in symptoms including tremor, stiffness, and impaired balance. A protein, Ubiquitin carboxyl-terminal hydrolase L1 (UCHL1) has been found to be related to the pathogen of Parkinson's disease and tumor progression. There have been novel inhibitors proposed that was theoretically computed to have a higher binding interaction to UCHL1 and we successfully synthesized those previously proposed inhibitors for protein UCHL1. Although these inhibitors are comparable to other known inhibitors and may not be the best, this is a step forward in understanding its interactions. Also, the computational study of the various analogues showed us that there is a substituent group effect that affects the binding between the inhibitor and UCHL1 protein. In our case, the general structure regarding the chlorine analogues at positions 2 and 3 yielded a lower delta G or better binding energy while positions 3 and 5 yielded a better binding energy for amine analogues.