Design, Synthesis, and Affinity of Dopaminergic Derivatives in SULT1A3

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Sulfation, an important metabolic process in the human body, is an essential pathway through which endogenous catecholamine and xenobiotic substances can be inactivated and/or have their solubility increased to facilitate removal from the body. The sulfotransferases (SULTs) catalyze the transfer of a sulfuryl group ($-SO_3^-$) from 3´-phosphoadenosine-5´-phosphosulfate to various substrate molecules. Of particular interest is SULT1A3 due to its role in the body and its specific substrate affinity for catecholamines, such as dopamine. In an effort to determine the molecular basis of its substrate selectivity of SULT1A3, a library of novel dopaminergic derivatives with various electron donating/withdrawing groups located at the 6 position were designed. The suite of compounds were analyzed in a computational model, synthesized, and studied in an enzymatic assay within SULT1A3. This study will discuss the methodology and results of each phase, both computational and experimental.