The prediction of reactive sites for nucleophilic and electrophilic attacks was investigated through frontier molecular orbital (FMO) analysis, Hirshfeld charges, and Fukui function (FF) calculations. The Fukui function was evaluated at the M06-2X/def-TZVP level of theory to identify the most probable reactive sites. The Fukui function is defined as:

$$f(r) = \left[\frac{\partial \rho(r)}{\partial N}\right]_v$$

where N is number of electrons in present system, the constant term in the partial derivative is external potential. For a given molecular system, Fukui function was calculated using electron density of three states:

$$f^+(r) = \rho_{N+1}(r) - \rho_N(r) \approx \rho^{LUMO}(r)$$

$$f^-(r) = \rho_N(r) - \rho_{N-1}(r) \approx \rho^{HOMO}(r)$$

$$f^0(r) = \frac{f^+(r) + f^-(r)}{2} = \frac{\rho_{N+1}(r) - \rho_{N-1}(r)}{2} \approx \frac{\rho^{HOMO}(r) + \rho^{LUMO}(r)}{2}$$

where N is the number of electrons in the current molecular system. The $N-1$ and $N+1$ states share the same molecular geometry as the N state. For nucleophiles, f^- is the reactivity descriptor, while for electrophiles, f^+ is the descriptor. f^0 is reactivity descriptor for radical attack. Atoms with larger Fukui function tend to have higher reactivities. Isosurface maps were produced using VMD 1.9.3 program based on outputs from the Multiwfn calculations.