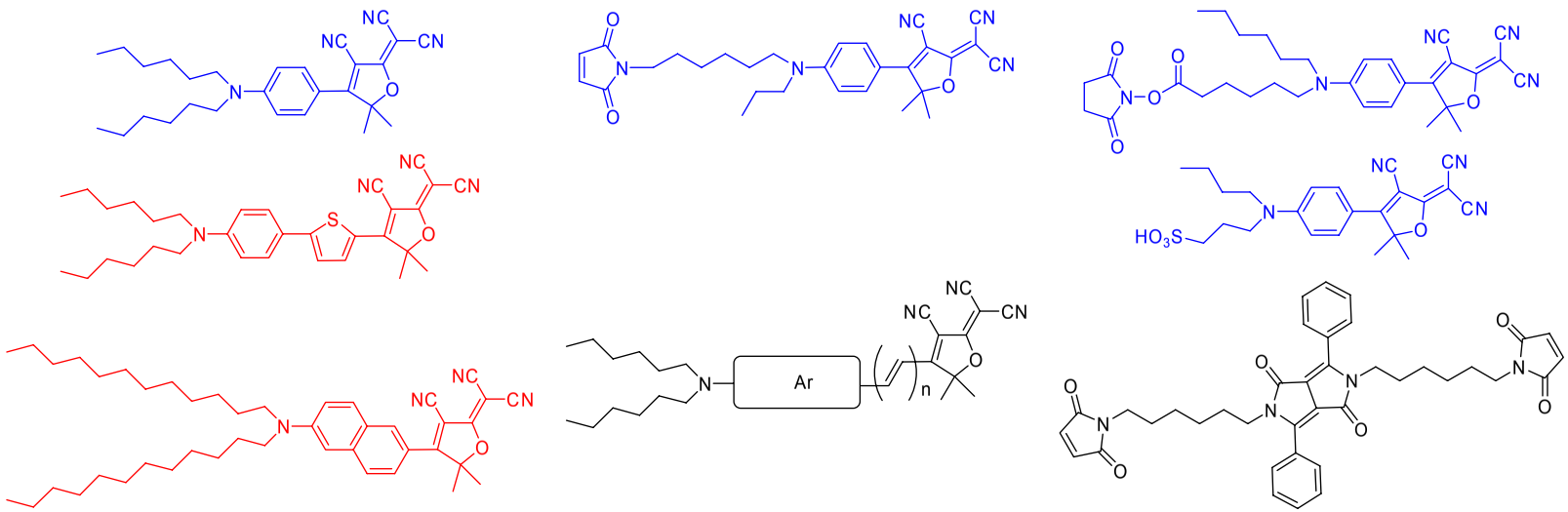
Design and Synthesis of Dicyanomethylenedihydrofuran (DCDHF) Single Molecule Fluorophores



Single-molecule imaging requires a strong and stable fluorescent emitter that can be detected at the single copy level. A family of molecules comprised of a dicyanodihydrofuran (DCDHF) acceptor and a dialkylamino donor linked by a conjugated unit have proved to be well suited for this purpose. In addition, this family of molecules also features other interesting physical properties including a ground state dipole moment and moderate hyperpolarizability. Structural opportunities exist for the modulation of absorption and fluorescence wavelengths and adjustment of environmental sensitivity/reporter function, solubility, hydrophilic and lipophilic properties. The original DCDHF fluorophores had a simple benzene or thiophene ring as the conjugated unit. We have recently introduced naphthalene, anthracene and various combinations of benzene and thiophene rings with resulting absorption and fluorescence shifted to longer wavelengths and with enhanced quantum yields. Reactive functional groups such as maleimides and succinimide esters have been introduced for protein labeling. Typical functional groups introduced to modify solubility and other properties include carboxylic acids, sulfonic acids, quaternary amines and alcohols. Other single molecule fluorophores, such as the DPP type (bottom left of figure) are also being investigated.