Performing selective reactions of compounds with multiple functional groups is a challenging objective, since each functional group can potentially adsorb and react on a catalytic surface. Addressing this problem is particularly important for the conversion of biomass to chemicals and fuels, because carbohydrates and their downstream intermediates contain multiple reactive functional groups. Our group has explored several techniques for aligning multifunctional molecules above metal surfaces to promote selective reaction of a particular functional group. One approach involves the modification of supported metal catalysts with organic ligands such as alkanethiols. Alkanethiols can be deposited on metal surfaces to form organized self-assembled monolayers (SAMs) that may cause reactants to adopt particular orientations above the metal surface, altering selectivity. At least two mechanisms by which SAMs can improve selectivity have been identified. First, SAM coatings can be used to tune the reactivity of the underlying metal surface sites. Second, the organic function of SAM coatings can be tuned to control non-covalent interactions in the near-surface environment. The utility of these two mechanisms for selectivity control will be illustrated for reaction chemistries important in biorefining and production of valuable chemicals. Some alternative directions for achieving surface and near-surface control will also be discussed.