as hydrophobic organic molecules, the two reagents would tend to form a separate layer, or at least form clusters of molecules, to release some of the low entropy water surrounding those hydrophobic groups — in the cluster of organic molecules, the effective concentration of reacts would be high (easy to fine one another) and so their reaction rate would increase.
in water, the exposed hydrophobic surfaces would be associated with a layer of low entropy water; spinning those groups around the water would be released AND have actual favorable interactions with the hydrophilic sides
The side chains of amino acids have lots of different properties related to noncovalent interactions: hydrophobic versus hydrophilic, acidic versus basic, sterically large versus small.

If an amino acid swap dramatically changes the properties of the side chain, then it might also affect the interactions taking place around it and change the conformation of the peptide chain or its interaction with its environment. The 3D shape of a protein is responsible for its behavior. Change the shape too much and the function also changes.

The change in function is not automatically negative. A mutation might also improve the function of the protein. If this improvement gives the organism a survival/reproductive advantage, then that positive mutation will also be passed on.