Carbohydrate−aromatic interactions are highly relevant for many biological processes. Nevertheless, experimental data in aqueous solution relating structure and energetics for sugar−arene stacking interactions are very scarce. Here, we evaluate how structural variations in a monosaccharide including carboxyl, N-acetyl, fluorine, and methyl groups a□ect stacking interactions with aromatic DNA bases. We find small di□erences on stacking interaction among the natural carbohydrates examined. The presence of fluorine atoms within the pyranose ring slightly increases the interaction with the C−G DNA base pair. Carbohydrate hydrophobicity is the most determinant factor. However, gradual increase in hydrophobicity of the carbohydrate does not translate directly into a steady growth in stacking interaction. The energetics correlates better with the amount of apolar surface buried upon sugar stacking on top of the aromatic DNA base pair.