

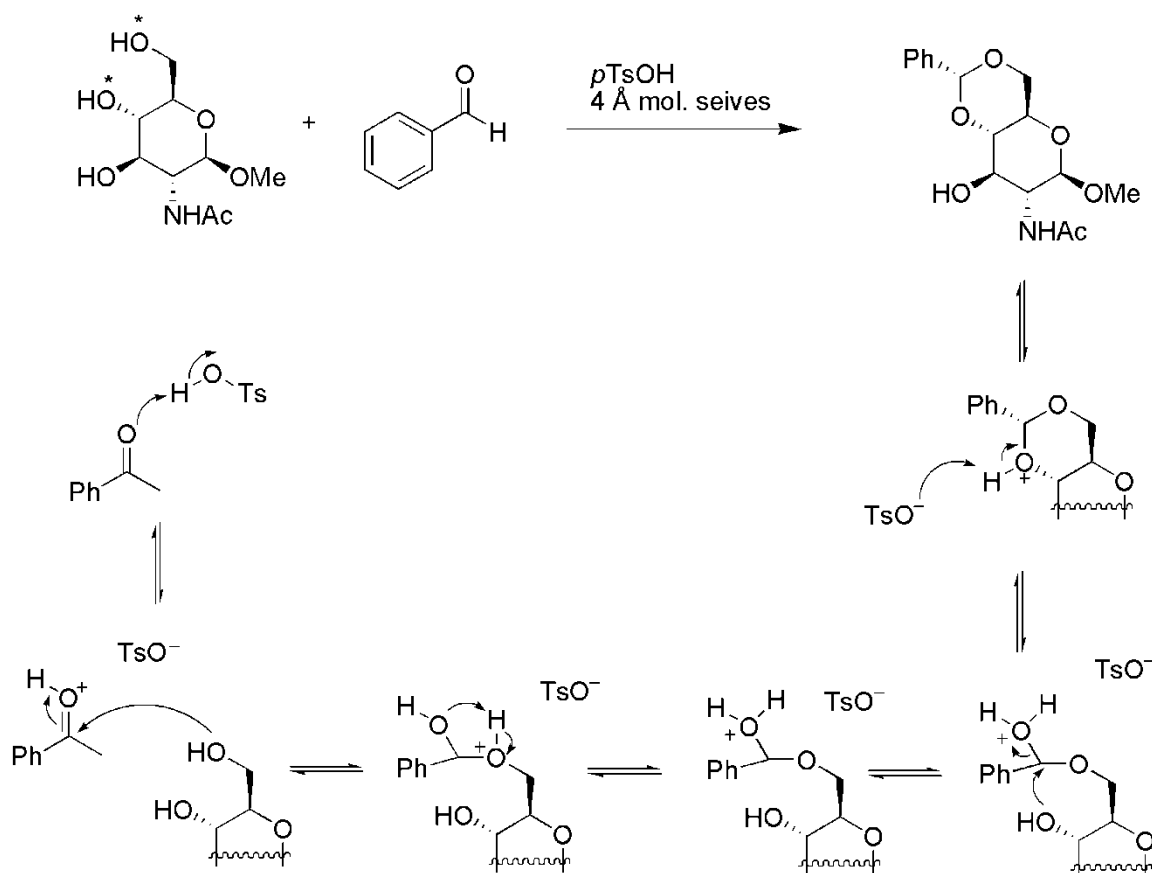
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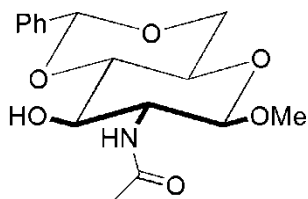
PS #7 - Orbitals and Conformations: Sugars and the Anomeric Effect

Part A) Recall that aldehydes can be protected by reaction with diols to form cyclic acetals. Using similar reactivity, certain diols can be protected by reaction with aldehydes. The reaction below is a powerful protection method that leads to the selective protection of two alcohols marked with a * by a single equivalent of benzaldehyde. As a group, propose a detailed mechanism for formation of the cyclic acetal.



This particular reaction selectively produces the six-membered ring acetal, and not the five-membered ring acetal that would be formed if the other two neighbouring alcohols reacted instead. Products thus protected are extremely useful for further functionalization at the remaining unprotected alcohol.

Part B) Draw the product in a full 3-D representation. *Politely ridicule each other's chairs until all are perfect representations of the molecule's shape.*

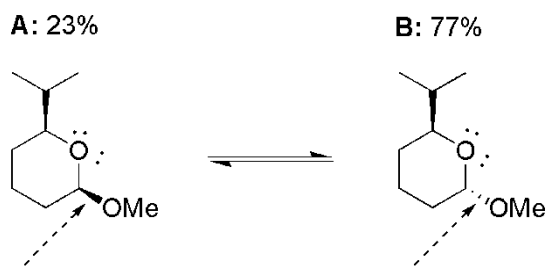


These trans-fused rings are structured essentially like a trans-decalin. Once your chair is well built, then focus on depicting a realistic structure by placing the equatorial substituents parallel to existing bonds. Notice that the phenyl substituent is installed using reversible steps. Thus the more stable product, having an equatorial phenyl group, is dominant.

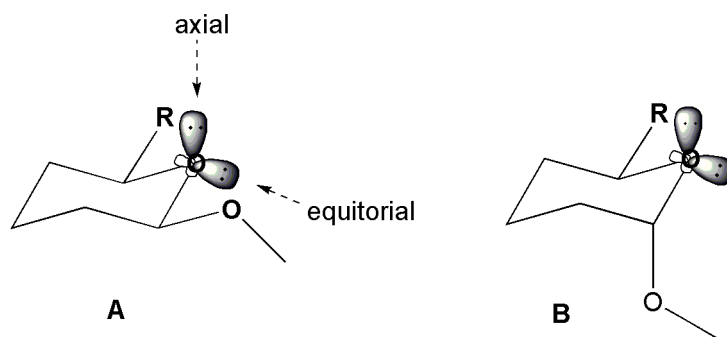
Part C) There is another acetal product that could be formed in the above reaction. The two vicinal alcohols could have reacted with benzaldehyde resulting in the formation of a five-membered ring. This would be the product predicted by Baldwin's rules for the rates of ring closing reactions. Obviously rates don't matter here... how is it that the 6-membered ring is the observed product?

The other possible acetal product would be a five-membered ring. Although five-membered rings form much faster (ie. they are the kinetic product), the six membered ring is the thermodynamically favorable product. Remember that acetal formation is reversible and in equilibrium. This results in formation of the thermodynamic product.

Part D) The sugar-like compound below can actually equilibrate between the two diastereomers shown (the mechanism involves acetal hydrolysis and re-formation, but it is unimportant for this question). The isomer at right (**B**) is favoured. *The origin of this effect commonly observed for sugar-like saturated heterocycles lies in a consideration of orbital alignment.*

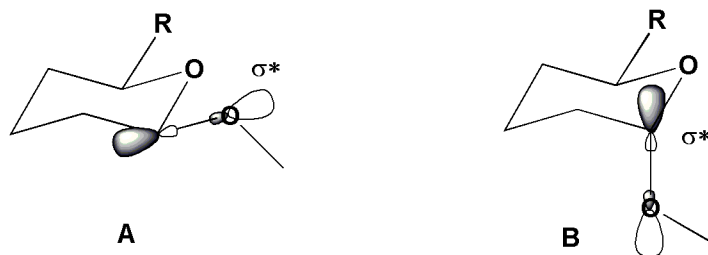


What kind of hybrid orbitals are the ring oxygen's lone pairs occupying? Draw the compounds in realistic 3-D representations that includes the geometries of the lone pairs.

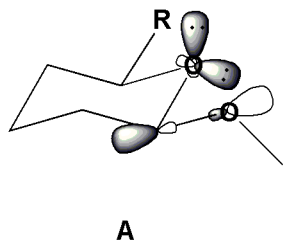


Oxygen's lone pairs occupy sp^3 non-bonding orbitals.

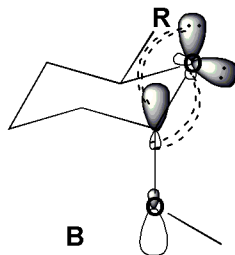
Now do the same for the σ^* antibonding orbitals of the bonds indicated by arrows.



Why is **B** more stable than **A**? Use pictures and a brief note to explain.



No parallel alignment of orbitals in **A**.



Parallel alignment of axial lone pair orbital and σ^* orbital. Electron density is donated via hyperconjugation, making this more energetically stable than compound **A**.

This effect is observed for many heterocycles with electronegative substituents at the position immediately next to a ring heteroatom. It was first observed in a series of sugars, and that neighbouring position in sugars is called "the anomeric centre". Thus, this stereoelectronic effect is called "the anomeric effect" to reflect its origins.