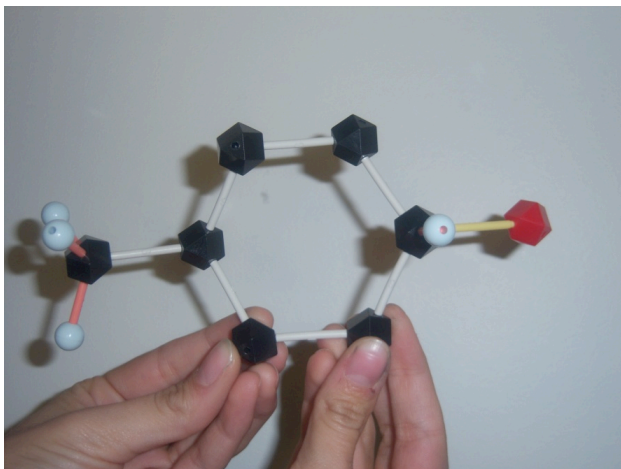


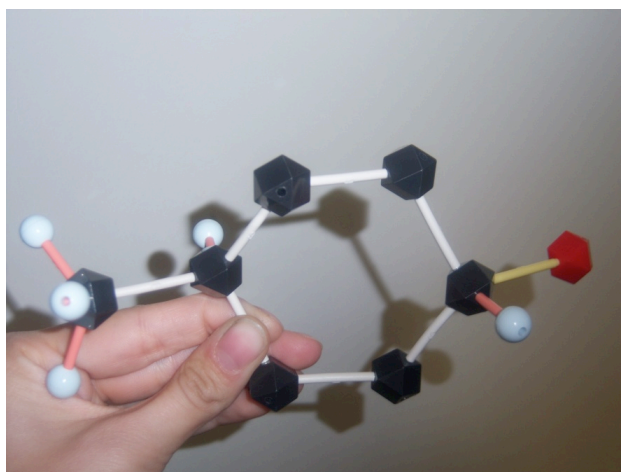
Molecular Model Kit Tutorial: How to Use Your Model Kit to Determine Stereochemistry in S_N2 Reaction Mechanisms

Based on a Chemistry 14D extra credit project, Fall 2008

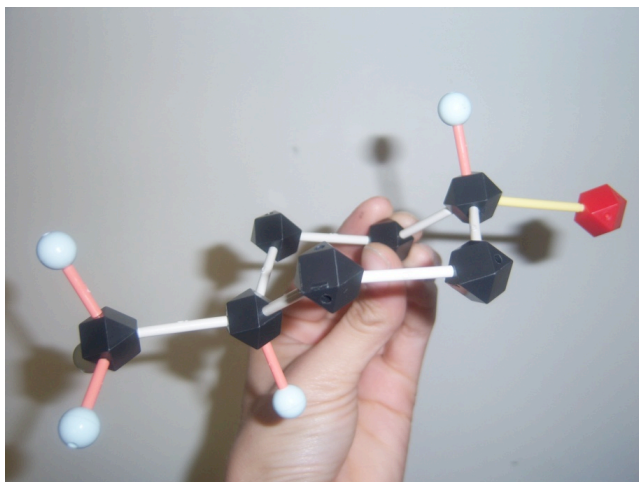


S_N2 reactions involve a bimolecular nucleophilic substitution at an sp^3 carbon where the bond between the carbon and the leaving group is broken and a bond between the carbon and the nucleophile is formed. Due to the electron density of the leaving group, the nucleophile “attacks” the carbon from its “backside,” to form a bond with the σ^* orbital that is available. The incoming electron density of the nucleophile also causes the substituents bonded to the carbon to undergo inversion, a complete “umbrella flip” of stereochemistry.

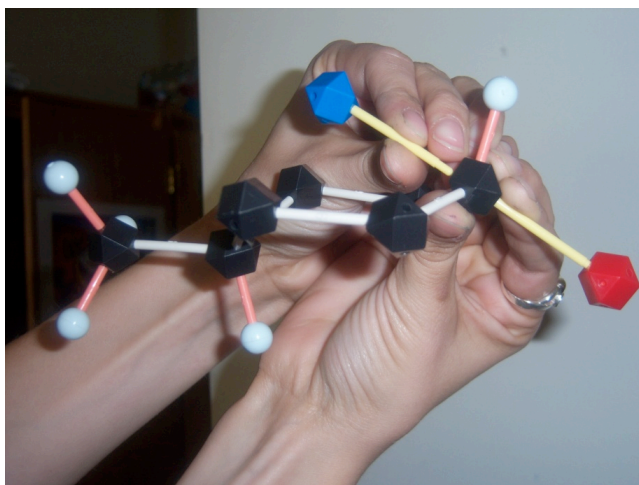
Here is an example of an S_N2 reaction. Above we have a cyclohexane ring with a methyl group and a chlorine atom bonded to the ring.



Above, we can see that the chlorine is facing away from us (red) and the hydrogen towards us.

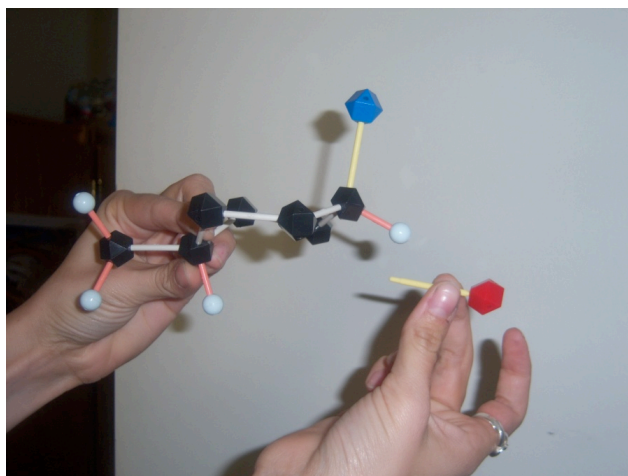


Here is a view of the molecule in chair formation, which is favored due to stability and can make it easier to visualize and draw the transition state of the reaction.

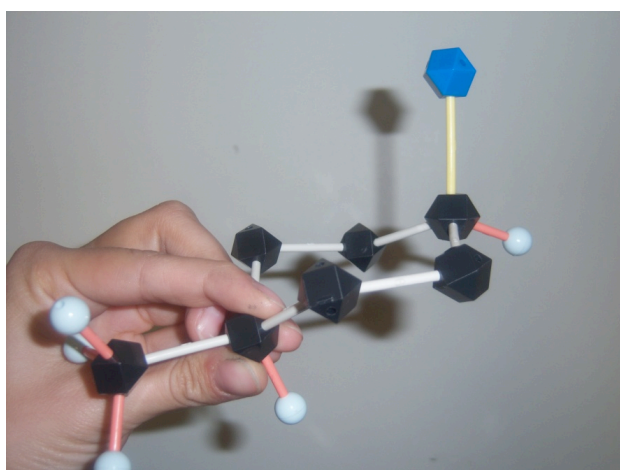


The nucleophile, iodide, approaches from the opposite side of the leaving group, chloride, as can be visualized by your molecular model. The solvent acetone is ideal for this reaction due to its lower polarity, which stabilizes the partial charges of the transition state more than the formal charges of the reactants and aproticity, which alleviates the hindrance of hydrogen bonding with the nucleophile.

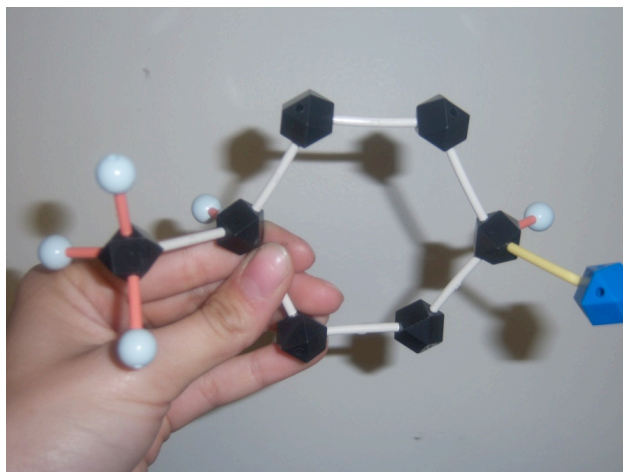
The transition state of the reaction is the highest energy structure of the concerted mechanism (bond scission and formation occurring in the same step). In the transition state, the C-LG bond being broken and the C-Nu: bond being formed simultaneously are drawn as a straight axis, and are dashed lines, indicating their partial scission and formation. The iodide and chloride both have δ^- charges, the leaving group (Cl) becoming more negative as it accepts the electron pair from the C-LG bond, and the nucleophile (I^-) partially losing its negative charge as it donates an electron pair to form a bond with the carbon.



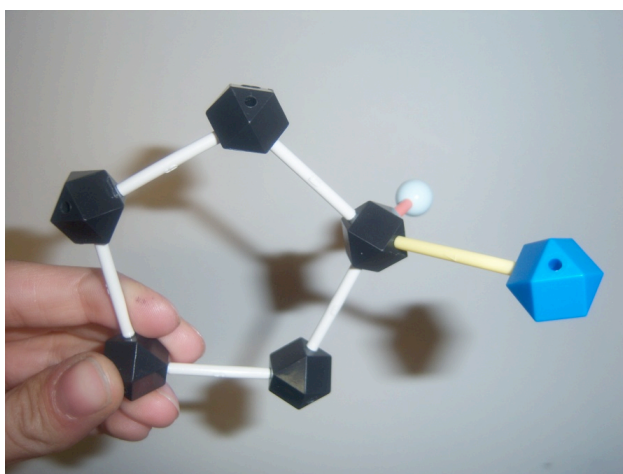
Due to the electron density of the nucleophile, the hydrogen atom of our model is repelled, and moves to replace the orientation previously held by the leaving group, which can be seen departing in the image above.



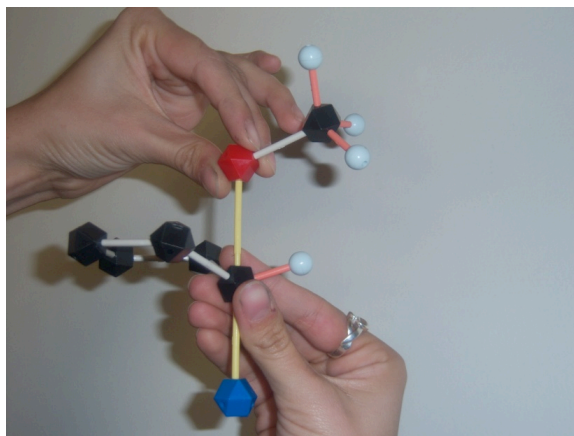
The final result of this is the inversion of stereochemistry at the carbon. In other words, *R* is flipped to *S* stereochemistry and vice versa.



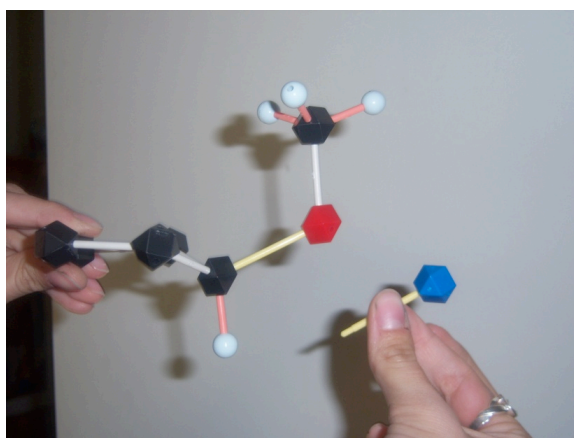
Here we can clearly see that inversion of stereochemistry has taken place, when compared to our original structure. Iodine is now facing towards us, and hydrogen away from us. Yay!



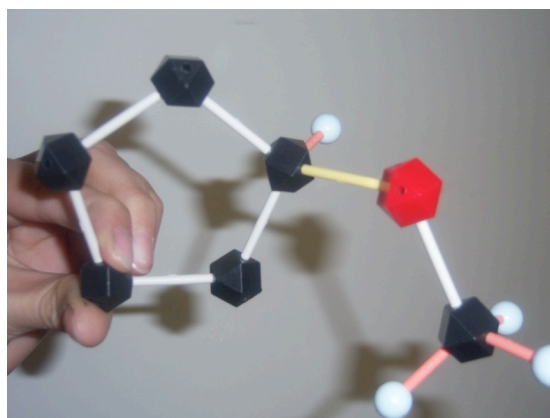
Here is another example: The leaving group of this cyclopentane molecule is chlorine, which becomes chloride ion, and the nucleophile is CH_3S^- , which is good for this reaction because sulfur has a low electronegativity, and cannot form hydrogen bonds in the protic solvent methanol as easily due to its large atomic radius.



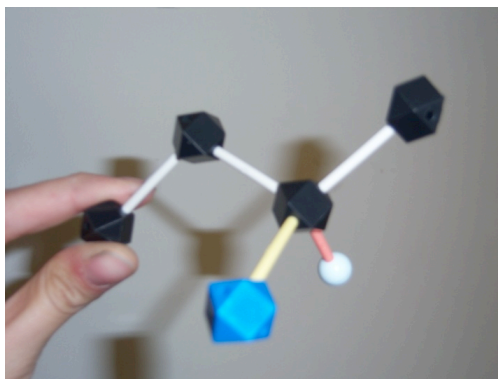
The nucleophile bonds with the electrophile through backside attack, forming a straight axis in the transition state, as depicted above.



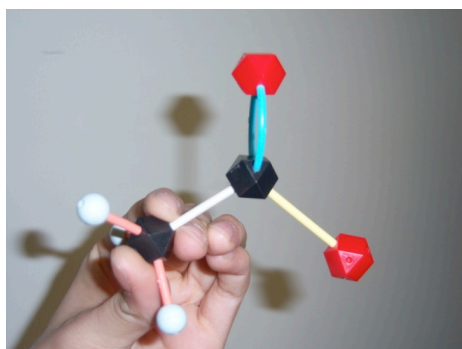
The C-LG bond is broken and the leaving group departs as chloride ion.



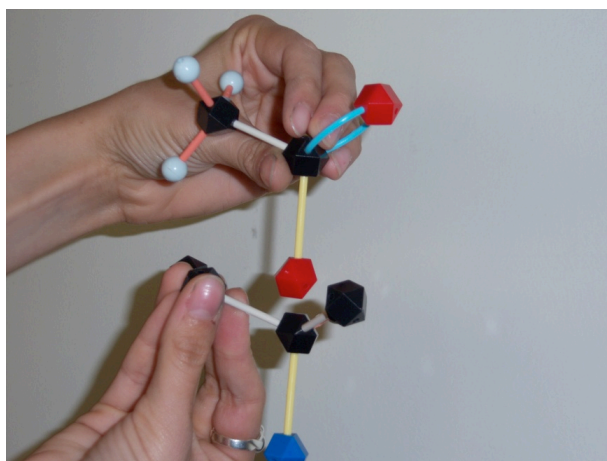
As we can see here, CH_3S^- has replaced the chlorine.



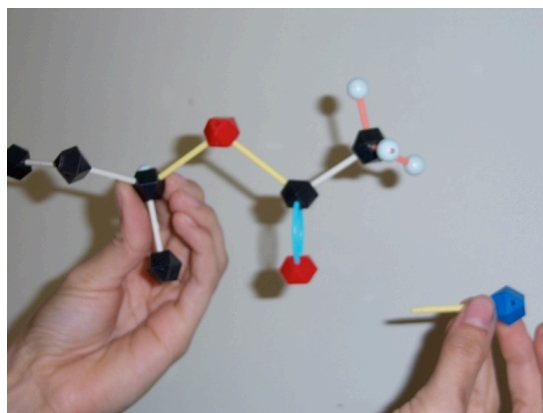
Here is a final example. See if you can identify the leaving group and imagine what the transition state will look like! Black=carbon White=hydrogen Blue=iodine



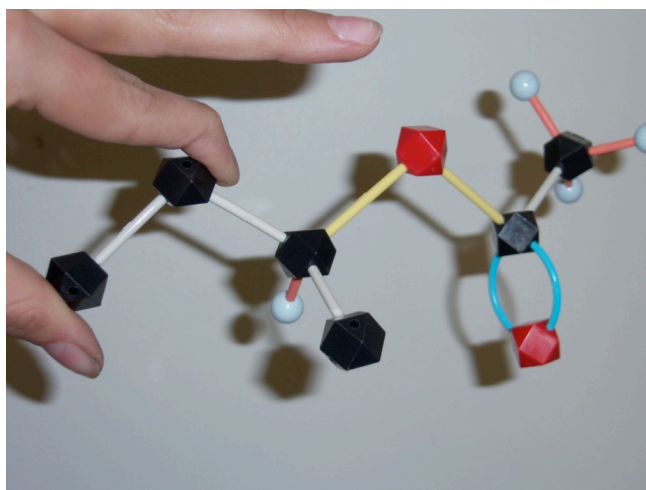
Here is a good picture of our nucleophile. Can you identify where the nucleophile will “attack” the carbon? (Hint: where is there an excess of electron density? Where is there a negative charge?) Black=carbon Red= oxygen White=hydrogen



Due to an excess of electron density on the oxygen with only one bond, this is where the nucleophile attacks the carbon. The bonds simultaneously forming and breaking again form a straight axis, which can be drawn in the transition state.



The leaving group (iodide) has departed, and due to the electron density of the nucleophile, and the methyl group has shifted to replace the orientation of the leaving group.



All done! As we can see, the stereochemistry at the carbon has been inverted, the methyl is now pointing towards us, and the hydrogen away from us!

Try other examples with your own model kit, it will help you to understand organic chemistry in a whole new light! Have fun!