

## 7.7: STEREOCHEMISTRY OF THE S<sub>N</sub>2 REACTION

### Learning Objective

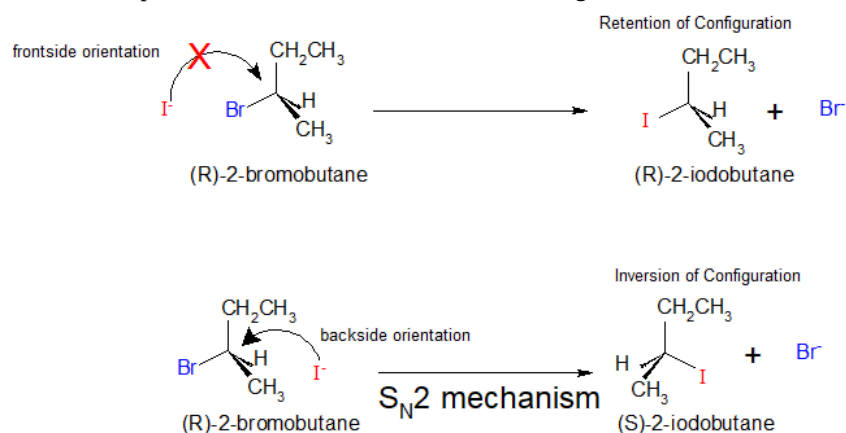
- predict the products and specify the reagents for S<sub>N</sub>2 reactions with stereochemistry
- propose mechanisms for S<sub>N</sub>2 reactions
- draw and interpret Reaction Energy Diagrams for S<sub>N</sub>2 reactions

### S<sub>N</sub>2 REACTIONS ARE STEREOSPECIFIC

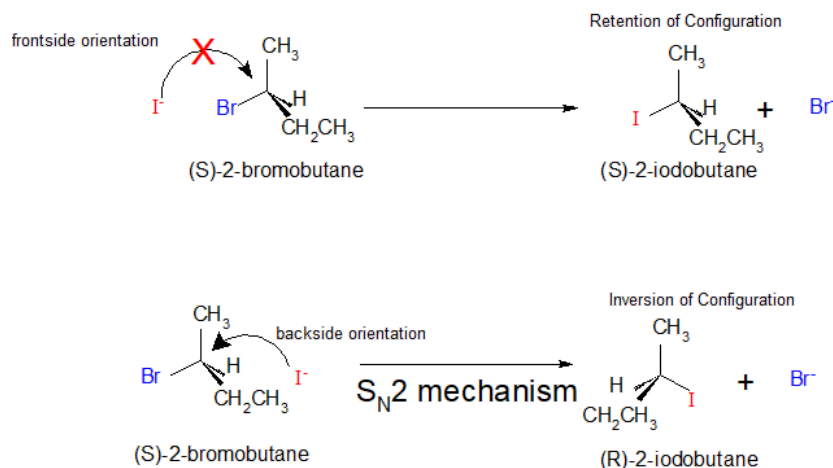
The S<sub>N</sub>2 reaction is stereospecific like other concerted reactions. A stereospecific reaction is one in which different stereoisomers react to give different stereoisomers of the product. The nucleophile and electrophile must be correctly oriented for orbital overlap to occur and trigger chemical reactivity. Experimental observations show that all S<sub>N</sub>2 reactions proceed with inversion of configuration; that is, the nucleophile will always penetrate from the backside in S<sub>N</sub>2 reactions. To think about why this might be true, remember that the nucleophile has a lone pair of electrons to be shared with the electrophilic carbon center and the leaving group is going to take a lone pair of electrons with it upon leaving. Because like charges repel each other, the nucleophile will always proceed by a backside displacement mechanism.

- **Frontside Orientation:** In a frontside orientation, the nucleophile approaches the electrophilic center on the same side as the leaving group. With frontside orientation, the stereochemistry of the product remains the same; that is, we have retention of configuration.
- **Backside Orientation:** In a backside orientation, the nucleophile approaches the electrophilic center on the side that is opposite to the leaving group. With backside orientation, the stereochemistry of the product does not stay the same. There is inversion of configuration.

For example, if the substrate is an R enantiomer, a frontside nucleophilic orientation results in retention of configuration, and the formation of the R enantiomer. A backside nucleophilic orientation results in inversion of configuration, and the formation of the S enantiomer.



Conversely, if the substrate is an S enantiomer, a frontside nucleophilic orientation results in retention of configuration, and the formation of the S enantiomer. A backside nucleophilic orientation results in inversion of configuration, and the formation of the R enantiomer.



Empirically, S<sub>N</sub>2 reactions that begin with the R enantiomer as the substrate will form the S enantiomer as the product. Those that begin with the S enantiomer as the substrate will form the R enantiomer as the product. This concept of retention and inversion of configuration

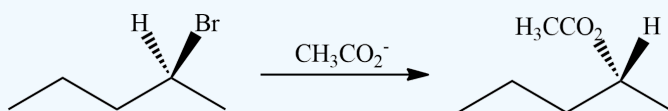
can also be applied to substrates that can exist as geometric isomers (*cis* and *trans*). If the *cis* configuration is the substrate, the resulting product will be *trans*. Conversely, if the *trans* configuration is the substrate, the resulting product will be *cis*.

### Exercise

1. Predict the product of a nucleophilic substitution of (S)-2-bromopentane reacting with  $\text{CH}_3\text{CO}_2^-$ . Show stereochemistry.

Answer

1.



### CONTRIBUTORS AND ATTRIBUTIONS

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