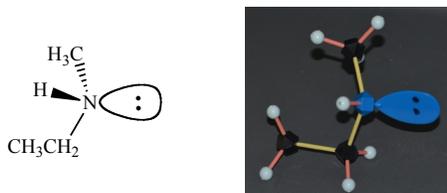


Nitrogen Inversion

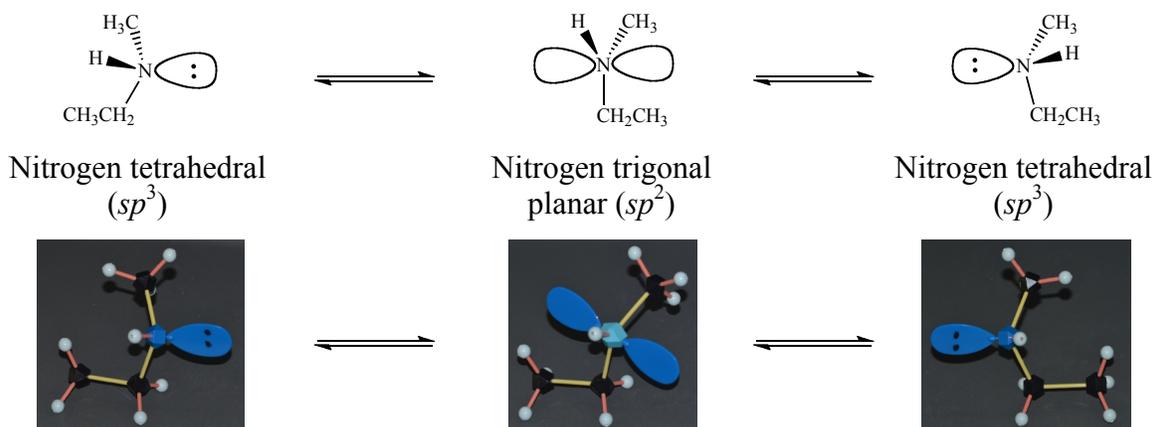
Goal: In this tutorial we'll learn about nitrogen inversion, and its consequences for nitrogen as a stereocenter. You'll need a good background in hybrid orbitals, stereochemistry vocabulary, and model kit use for this tutorial. If you feel less than 100% confident in any of these areas, now would be a good time to review the corresponding tutorials available at the course web site.

Nitrogen Inversion: What Is It?

An amine such as ethyl methyl amine has a tetrahedral (sp^3) nitrogen atom, and the nitrogen lone pair in an sp^3 orbital. (You'll gain a greater appreciation for the concepts in this tutorial if you build models of the structures shown.)



However this tetrahedral amine structure is not static. In 1934 it was discovered that the nitrogen atom inverts. The lone pair disappears from one face, moves through the nucleus, and reappears on the opposite face. (This magical act is called quantum mechanical tunneling.) The lone pair repels the ethyl group, the hydrogen atom, and the methyl group, so as the lone pair reappears, these groups move away. As the lone pair is tunneling through the nucleus, the nitrogen has just three attachments so this nitrogen atom is trigonal planar with sp^2 hybridization.



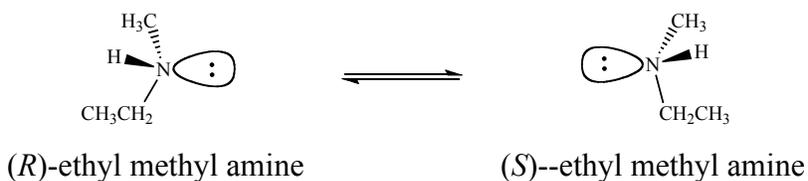
The tetrahedral amine structures are in equilibrium. Furthermore, these structures are enantiomers. (Verify with your model kit.) All physical properties of enantiomers are identical (except for the direction in which they rotate plane polarized light). From this we can conclude that the two amine enantiomers have equal stability (they are present in equal amounts), and so the inversion $K_{eq} = 1$.

Why Does Inversion Occur?

Inversion occurs because an atom has a lone pair. So in principle many molecules could invert, but laboratory measurements have shown that only in the case of nitrogen is barrier to inversion low enough for inversion to occur at an observable rate. Rapid lone pair tunneling and inversion is unique to nitrogen. Other elements with one or more lone pairs, such as phosphorous or sulfur, either invert only very slowly, or not at all.

Consequences for Nitrogen as a Stereocenter

A tetrahedral nitrogen atom with four different attachments (such as the lone pair, hydrogen atom, ethyl group, and methyl group in our current example) is a stereocenter. We can assign absolute configuration to the amine enantiomers. (A lone pair has no protons, so therefore has atomic number = 0, and the lowest Cahn-Ingold-Prelog priority.) Verify the absolute configurations shown below with your model kit.



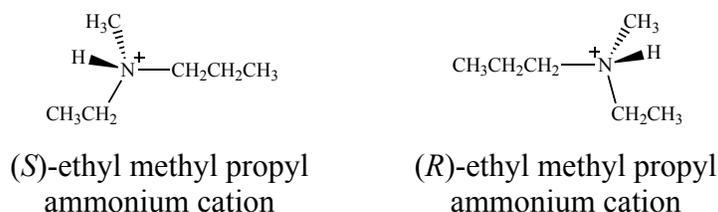
These amine enantiomers have equal but opposite optical activity, so in the 1:1 equilibrium the mixture is racemic, and optically inactive.

It is because of this facile inversion and racemization that we usually do not consider a nitrogen atom (even with four different attachments) as a stereocenter. However, not all nitrogen atoms can invert readily, so in some cases a nitrogen atom can be a stereocenter.

When Can Nitrogen Be a Stereocenter?

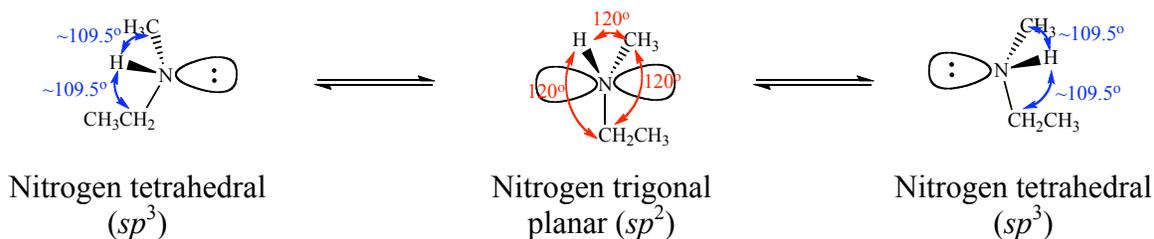
There are two circumstances in which a nitrogen atom cannot invert, and therefore might be a stereocenter.

Circumstance #1: No Lone Pair. Nitrogen inversion occurs because of lone pair tunneling. In the absence of a lone pair, no inversion occurs. When a nitrogen atom has four σ bonds (in an ammonium cation), inversion is prevented. Therefore if a nitrogen atom has four different attachments and no lone pair, the nitrogen atom is a stereocenter, and the molecule has all the properties normally expected when a stereocenter is present (enantiomers, optically active, etc.). For example, the ethyl methyl propyl ammonium cation is chiral.

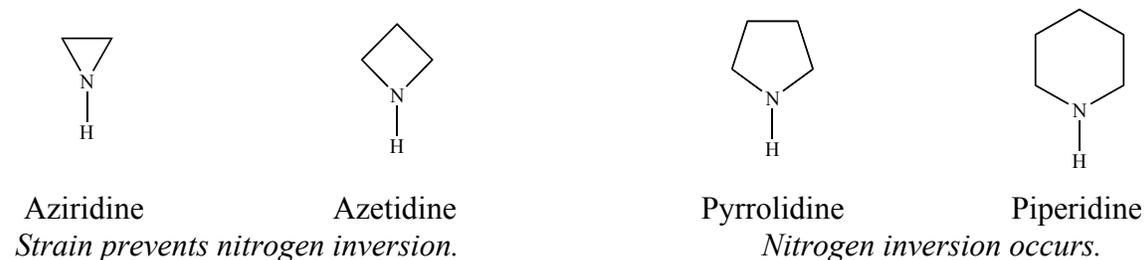


Use your models to verify these absolute configurations, and to verify that these cations are enantiomers.

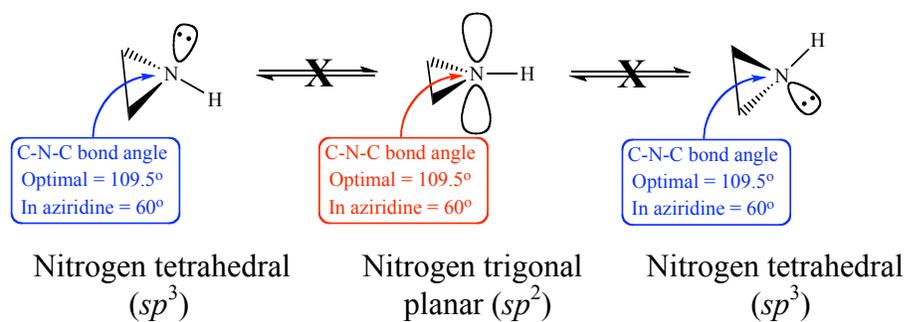
Circumstance #2: Ring Strain. When the nitrogen atom of ethyl methyl amine is tetrahedral (sp^3), the C–N–C or C–N–H bond angles are approximately 109.5° . As the lone pair tunnels through the nitrogen atom nucleus and the structure becomes planar (the nitrogen is sp^2) the C–N–C and C–N–H bond angles change from $\sim 109.5^\circ$ to 120° . As the lone pair emerges again, the groups continue their motion, and the structure resumes its tetrahedral shape with $\sim 109.5^\circ$ bond angles.



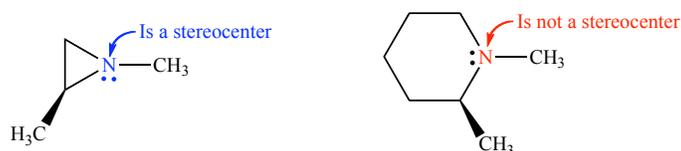
When the amine nitrogen is not part of a ring, this bond angle change is easily accommodated. However, if the nitrogen atom is part of a three-membered ring (called an aziridine) or a four-membered ring (called an azetidene) inversion is significantly retarded by strain.



For example in an aziridine, before inversion the nitrogen atom already experiences significant angle strain (109.5° optimal tetrahedral C–N–C bond angle versus the 60° actual bond angle in the ring). The strain is at its worst when in the planar intermediate structure: 120° optimal trigonal planar C–N–C bond angles versus 60° actual bond angle in the ring). The increase in strain makes it too difficult for the inversion to occur, and the aziridine nitrogen atom can be a stereocenter. Verify this with your model kit but be careful...the strain may break some of the bond sticks!



The situation is similar (although somewhat less severe) in an azetidine. In larger rings, such as a pyrrolidine ring or a piperidine ring, the strain increase required for inversion is less. Inversion can occur, and these nitrogens are not stereocenters.



Aziridine and azetidine rings are not the only cases in which strain may prevent nitrogen inversion. Evaluate each case individually, and make a judgment call. For example, quinuclidine is a case in which the nitrogen atom is in a six-membered ring, but cannot invert due to the impossible geometry that would result.



More Reading: http://en.wikipedia.org/wiki/Nitrogen_inversion