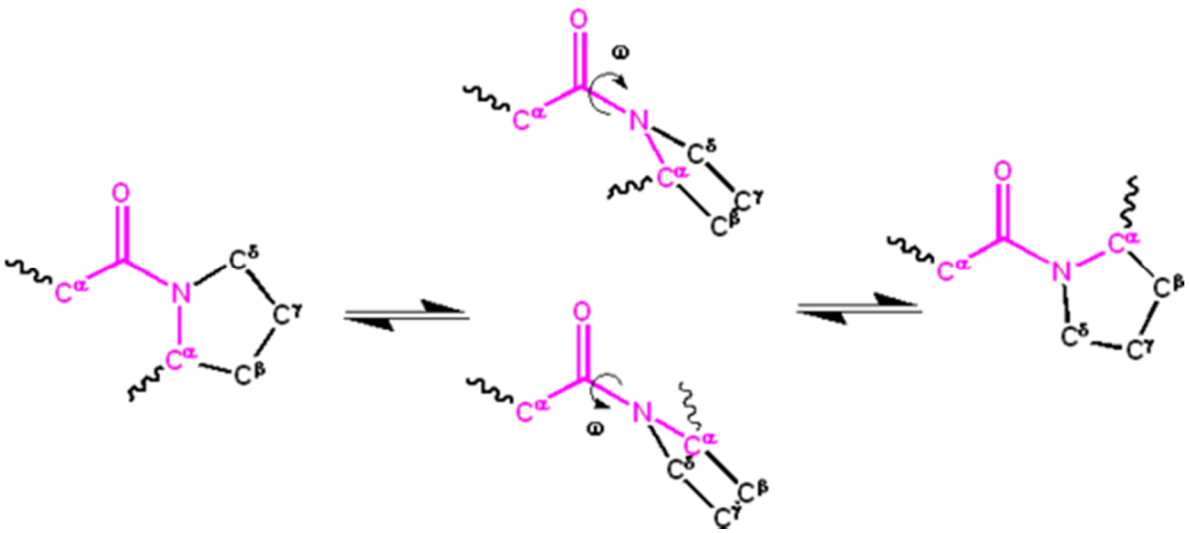
Question#46144 – Chemistry – Other

Question:

Describe the stereochemistry of the peptide bond and explain how this is significant in restricting the number of conformations of a polypeptide chain.

Answer:

Significant delocalisation of the lone pair of electrons on the nitrogen atom gives the group a partial double bond character. The partial double bond renders the amide group planar, occurring in either the cis or trans isomers. In the unfolded state of proteins, the peptide groups are free to isomerize and adopt both isomers; however, in the folded state, only a single isomer is adopted at each position (with rare exceptions). The trans form is preferred overwhelmingly in most peptide bonds (roughly 1000:1 ratio in trans:cis populations). However, X-Pro peptide groups tend to have a roughly 3:1 ratio, presumably because the symmetry between the C^{α} and C^{δ} atoms of proline makes the cis and trans isomers nearly equal in energy (See figure, below).



The dihedral angle associated with the peptide group is denoted $\omega = 0^{0}$ for the cis isomer and $\omega = 180^{0}$ for the trans isomer. Amide groups can isomerize about the C-N bond between the cis and trans forms, albeit slowly .The transition states $\omega = 90^{0}$ requires that the partial double bond be broken, so that the activation energy is roughly 80 kilojoule/mol (20 kcal/mol). However, the activation energy can be lowered (and the isomerization catalyzed) by changes that favor the single-bonded form, such as placing the peptide group in a hydrophobic environment or donating a hydrogen bond to the nitrogen atom of an X-Pro peptide group. Both of these mechanisms for lowering the activation energy have been observed in peptidyl prolyl isomerases (PPIases), which are naturally occurring enzymes that catalyze the cis-trans isomerization of X-Pro peptide bonds.

Conformational protein folding is usually much faster (typically 10–100 ms) than cis-trans isomerization (10–100 s). A nonnative isomer of some peptide groups can disrupt the conformational folding significantly, either slowing it or preventing it from even occurring until the native isomer is reached. However, not all peptide groups have the same effect on folding; nonnative isomers of other peptide groups may not affect folding at all.