CHAPTER 6

CONCLUSIONS

1. Optimised geometrical structures of substituted tetrazoles predict bond lengths of the ring system very close to the unsubstituted tetrazole. The electron donating and withdrawing properties of the selected substituents influence the tetrazole only to a small extent. Therefore, the strong resistance of substitution effects and the ring to subsequently potential geometrical alterations cannot be negated arbitrarily.

2. Ease of tautomeric transformation is not improved by the electronic effects of the selected substituents on tetrazoles. Since the calculated activation barriers for all the substituted isomers do not show large change from the unsubstituted compound, the expectation of the role of substituents to electronically affect the predominant 2H-tautomer supports the inherent nature of the ring under normal condition in the gas phase. Also, lowering of singlet-triplet energy gaps and HOMO-LUMO energy gaps were predicted upon substitutions, the influence of substituents were not strong enough to enhance tautomerisation in the gas phase because of the persistent nature of the ring.
3. The influence of substituents on the tetrazole systems in terms of thermodynamic equilibrium constant relating to the Gibbs free energy change predicted deviation from the unsubstituted compound. Base on the calculated results, electron donating groups tend to decrease the equilibrium constant as compare to the unsubstituted compounds, whereas substitution with electron withdrawing groups result in the increase of equilibrium constant. Thus, although substituents do not impart significant change on the geometry of tetrazole ring, the energetic contribution from the substituents cannot be completely ignored.

4. The calculated values of HOMA and I_5 which suggested small change in the degree of aromaticities of substituted tetrazoles from the unsubstituted tetrazole, is in compliance with the electronic resistance to the substituents. The calculated geometry based index of aromaticity also serves as evidence in establishing higher aromaticity of 2H-tautomer over the 1H-tautomer, and also support any previous study showing the predominance property of 2H-tautomer over 1H-tautomer. Thus, the strong electronic resistance of the tetrazole ring to the substituents results in a small change in the degree of aromaticity with respect to the unsubstituted tetrazole since HOMA and I_5 are structure based indices for aromatic criteria.

5. The influence of substituents to the magnetic properties of tetrazole are very low. Computation of NICS values reveals that influence of substituents on the π-electron delocalization of the tetrazole ring were not high. These suggested that substituents effect meets resistance to the change in π-electron delocalization in the ring. Also, the distribution of π-electron density is higher at the centre of the ring than above plane of the ring.

6. 2H-tautomer is energetically preferred over the 1H-tautomer in the case of 1,2,3-triazole while 1H-tautomer was predicted more stable than 2H-tautomer in 1,2,4-triazole isomers.

7. 1,2,4-triazole tautomers were found to differentiated by small energy differences in the gas phase and this suggested the possibilities of thermoneutral reaction or an isodesmic transformation between 1H- and 2H-tautomers of 1,2,4-triazoles. cannot be downrightly rejected in the transformation of 1,2,4-tautomers.

8. 1,2-prototropic shift in favor of tautomerisation process was found to be governed by high energy barriers, and these barriers were not affected much by the influence of substituents (-NO_2 and -CH_3) according to the energetic properties from singlet-triplet energy gaps and HOMO-LUMO energy gaps in triazoles, although ground state energies were increase with substitutions.

9. High degree of aromaticities with respect to their magnetic properties were predicted for both the 1,2,3-triazole and 1,2,4-triazoles isomers as well as for their transition state species.

10. Acyclic transition state geometries were predicted for the migrations of hydroxy group in triazole isomers. Prediction of high activation barriers were seen in both the isomers, and zero difference in ground state total energies were obtained for 1,2,4-triazole.

11. Stereo structures of triazole is well preserved in letrozole and vorozole compounds and high ground state energies are predicted for both the triazole derivatives.

12. Different combination of model chemistries predicted different total energies for letrozole and vorozole, an inclusion of MM methods were found to predict lower total energy, while introduction of QM/QM results in higher total energy.

13. Computationally, consistency seems to preferred DFT method while lower cost of computational time was achieved with HF method, and 6-311++G(d,p) was the most efficient among the basis sets in this research work on 5-membered N-heterocycles.