# Chapter 7

## Conclusions

*Comprehensive conclusions of this dissertation are presented here.*

# Conclusions

This chapter portrays summary and concluding remarks of all the preceding chapters of this thesis. Here we have emphasized on the theoretical exploration of organic reactions. In this vast area of knowledge we have selected to cram the addition reactions. In chapter one there is a general introduction about the theoretical analysis of addition reactions. The background of the present thesis is elucidated here. At the very beginning, we have discussed the addition reaction-its definition, types and mechanism. Finally, we have discussed about the scope of applications and various mechanistic aspects of addition reactions. The objectives of this thesis are also categorically described.

Chapter two deals with the theoretical platform for the calculation of electronic energy, charge density and potential energy surface of different species involved in a reaction. We have discussed the theoretical setting for calculation of transition state with the help of Born-Oppenheimer approximation. The background for the prediction of reactivity of a molecule towards an attacking reagent is also conferred here.

In chapter three, we have investigated the electrophilic addition of benzene (monoprotonation, diprotonation, monomethylation & dimethylation) in DFT framework using UB3LYP hybridfunctional with the 6-311++G(d, p) basis function. The results reflect the same trend of mechanistic pathways for diprotonation and dimethylation reactions. For both the reactions, the most stable product is a meta disubstituted one followed by ortho and para isomers. It is also evident from simple valence bond based qualitative approach. In this approach, one can readily find only one possible structure for para disubstituted product in which two positive charges are geminal. In ortho and meta disubstituted products two resonating structures could be found; however, in case of ortho in one of these structures again charges are on neighboring sites, whereas, in case of meta isomer in none of them charges are adjacent. This clearly points out the meta disubstituted product to be most favorable energetically followed by ortho and para. This is also supported by local charge density values. Nevertheless, in case of diprotonation

reaction the para isomer has been found to be kinetically controlled product whereas the ortho one is the same for dimethylation reaction. Fukui function and local softness have been found to be good descriptors for kinetically controlled product. Proton affinities and methyl cation affinities have been found to be additive in nature and these values justify the calculated thermochemical parameters. A correlation is observed between proton and methyl cation affinity with the change in enthalpy.

In the forth chapter, we have studied the addition mechanism of two molecules of 1, 3-dicarbonyl compound and one molecule of aldehyde in presence of molecular iodine within unrestricted DFT framework using B3LYP hybrid functional. General steps of the reaction are studied using acetyl acetone as 1, 3-dicarbonyl compound and acetaldehyde. There may be two pathways depending on the substitution pattern of 1, 3-dicarbonyl compound. One leads to spiro dihydrofuran and other cyclopropane derivatives. Paths being followed in either situation can be predicted by condensed Fukui function calculation and by ESP analysis. In each steps transition states are calculated. Vibrational analysis, IRC calculations and ESP analysis authenticate these transition states. The nucleus independent chemical shift (NICS) calculation suggests that the gain in aromaticity plays an important role in the last step of the reaction. Thermochemical analysis is in good agreement with each step of the proposed mechanism. As a whole, the present DFT study explains well the experimental findings and also provides the details of the reaction mechanism.

Chapter five contains a benchmark study of the performance of different versions of the M05, M06 and M08 set of Minnesota density functionals with first row transition metal compounds. In this study, we have evaluated the accuracy and reliability of eight M0X suite of functionals for the prediction of HOF and IP values of different first row transition metal complexes. We have taken 54 benchmark TM complexes for calculating the HOF values, whereas only 47 systems among these molecules are taken for evaluating IP values due to lack of experimental results. It has been found that the M06-L functional is the best average performer among the M0X series of functionals in predicting thermodynamic parameters of different first row TM complexes, whereas the

robust functional M06-HF gives the worst performance in predicting such properties confirming the recommendation of the developers of these functionals that the Minnesota density functionals with high H-F exchange should not be used for the TM compounds. Nonetheless, almost similar performance is shown by the M06-2X, M08-SO and M08-HX functionals having closely HF exchange in treating the thermochemical parameters of the TMs. The Fe complexes show most notorious HOF results, whereas Ni complexes are found to be most problematic for the prediction of IP values. The discussion about the huge average HOF errors produced by the Fe complexes by our chosen eight Minnesota density functionals is due here. Notably, there are difficulties in dealing TM complexes by computational techniques due to the partial filling of *d* orbitals which is also responsible for degeneracy. In case of the prediction of IP values the deviation from the experimental results is much smaller than that of HOF results. Besides M06-L functional, the M05 and M06 functionals are also to be recommended for the theoretical prediction of these thermochemical parameters for the first row TM complexes. From the results obtained in this work, one can categorically extract the following points- (i) The non-hybrid meta GGA M06-L functional with zero exchange correlation energy outdo all other functionals in predicting unsigned HOF values of the respective species. (ii) In predicting the IP results the performance of the M06 functional is found to be even better than the results obtained from M06-L functional. (iii) The hybrid meta GGA M05 and M06 functionals show quite accurate results after the local one compared to the other hybrid functionals taken for this study. (iv) With the increase of exchange correlation energy the performance of the M0X group of functionals to predict these physical properties for different first row TM complexes is noticeably found to be lowered. (v) The M06-HF functional having cent percent exact exchange contribution gives huge deviated results in all the field of calculations used in this study. (vi) We conclude that the M05 and M06 functionals found to be the good alternative to the popular B3LYP functional to study the HOFs and IPs. (vii) Considering the signed and unsigned HOF and IP errors, one can find with ease that 3 out of 4 cases the performance which has made by M08-SO is considerably more accurate than its other M08 counterpart. Nonetheless, this study has two quite different aspects: (a) Testing of the functionals *viz.* M06-L, M05 and M06 which are excellent candidates for the transition metal

applications can forms a new transition metal database, and (b) Double checking the original recommendations that the functionals with $\chi > 30$ should not be used for transition metals. At last an interesting note is that all existing M0X family of functionals have their own strength as well as weaknesses, hence there lies a difficulty in choosing the right functional to evaluate a particular physical property. We hope that, upcoming years will see a new M0X functional with all the merits which all would exist in the today's M0X functionals.

In the sixth chapter, we have investigated the regioselective nitronium ion addition to 4-quinolones using DFT based reactivity descriptors. Fukui function and local softness are calculated for different model compounds. From theoretical analysis, we draw the conclusion that regioselectivity can easily be tuned by selective protection of free –NH group. Moreover our theoretical predictions are justified by experimental rationalizations. Good agreement was found when comparing the predicted regioselectivities with experimental data. Finally this selective nitration allows introduction of nitro group in the diverse position of the 4-quinolone ring and this study will definitely be useful for the target synthesis of new bioactive molecules based on the 4-quinolone system.