

Comparison of ortho and meta-positions of nitrobenzene for aromatic electrophilic substitution reaction

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Abstract: The approach of this theoretical work is to study the step by step mechanistic pathway of electrophilic substitution reaction in substituted benzene and evaluating energy of each species involved in the mechanism. Nitrobenzene was taken as substituted benzene, nitronium ion was taken as an electrophile while hydrogen ion (H^+) act as the leaving group. The nitro group present in the ring is an electron withdrawing group therefore its effect on electrophilic substitution of hydrogen from the ring system was taken into consideration. Quantum mechanical based computational calculation was employed for determining energy of molecular/ionic structures involved in the mechanism, where activation or deactivation of the ring by nitro substituent and its directing behaviour to the meta or ortho position for electrophilic substitution were also included for a part of the study. The study is based upon the energy calculation of different structures in the mechanistic pathway and calculation of activation energy for 1,2-shift in meta and ortho-positions.

Keywords: 1,2-shift, meta and ortho-positions, electrophilic substitution, mechanistic pathway, nitrobenzene, nitronium ion, activation energy.

1. Introduction:

Since aromatic compound has electrons delocalizing in the ring system, it can act as a nucleophile where electrophile can attack with its positive center or vacant orbital. There are four different reactive positions in a mono-substituted benzene. The ring carbon atom bearing the substituent is called ipso, the next ring carbon is ortho, the third position is meta and fourth position is Para.

Substituents are generally divided into two classes based on their electron donating and electron withdrawing properties. Activating groups stabilize the cationic intermediate formed during the substitution by donating electrons into the ring system by either inductive effect or resonance effects. On the other hand, deactivating substituents destabilize the intermediate cation by withdrawing electron density from the aromatic ring and thus decreases the rate of reaction.

In the first step of electrophilic substitution reaction, nucleophile attacks the aromatic ring at any one of different positions. This leads to the formation of a positively-charged cyclohexadienyl cation, also known as an arenium ion. This carbocation is unstable, owing both to the positive charge on the molecule and to the temporary loss of aromaticity. However, the cyclohexadienyl cation is partially stabilized by resonance, which allows the positive charge to be distributed over three carbon atoms. In the second stage of the reaction, a proton leaves the ring and the shared electrons return to the π system thus restoring aromaticity.

In electrophilic substitution reaction, hybridisation change is also observed at the carbon where new sigma-bond is formed between the incoming electrophile and the carbon which is being attacked. The orbital with sp^2 before the attack get changed to sp^3 after a new bond has been formed. After deprotonation sigma bond between carbon and hydrogen is broken and the sigma electrons get changed to pi-electron thus carbon reforms its sp^2 hybridised orbital.

2. Methodology:

Calculation of the gradient-corrected electron density function, geometries, energies and frequencies of different structures involved in the mechanisms was done by using the gradient-corrected hybrid B3LYP basis function with 6-31G* standard split valence basis set of the Density Functional Theory method of Gaussian 98 revision A.11.2 package. The transition state for the migration of nitronium ion from meta-C to ortho-C were located by using the standard saddle principle of the Gaussian 98 package, invoking a reverse search strategy with interpolation between the equilibrium geometries of the reactants and products to arrive at the transition state. Once located, the transition state was verified. Energy-minimized heats of formation were calculated for each of the molecular species involved in the mechanism and used as the basis for calculating the energy profile for the reaction pathways in each case.

The study of the reaction was based upon the energy involved due to steric interaction, angle strain, geometries, frequency, etc. Once the energy for each intermediate was calculated the feasibility of the reaction can be predicted. All the structures were calculated in the semi-empirical AM1 method and the Density Functional Theory (DFT) B3LYP/6-31g* levels of calculations and Hartree energies were obtained for all the cases. The Hartree energies were then all converted to the corresponding Kcal/mole where the first structures for all the cases were taken as zero and the rest of the structures were calculated with respect to the first structure for all the mechanisms studied.

3. Result and discussion:

Mechanism-A: This mechanism involves the attack of nitronium ion by the π -electron in the benzene ring at the meta-position as given in figure-1. Subsequently structure **II** loses its aromaticity, which is again regained by deprotonation in structure **III**. This

deprotonation process being facilitated by the electron-deficient carbo-cation center in the ring. Structure **II** gave rise to two resonating structures with different environments.

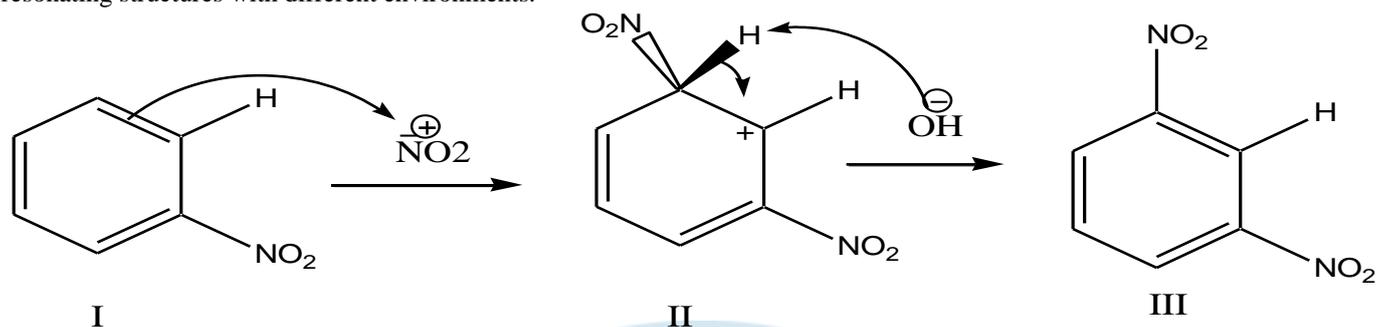


Figure-1. Mechanism-A showing the nitration of nitrobenzene at the meta-position and the deprotonation step.

Table-I. Energy calculated for each structure of mechanism A, total energy in hartrees and the relative energy in Kcal/mol.

Structure	AM1	RE	AM1 OPT	RE	B3LYP	RE
A-I	60	0	62	0	401814	0
A-II	380.8	320.8	257	195	402283	469
A-III	128	68	92	30	402123	388

Mechanism-B: The second mechanism begins with the attack at the ortho-position to the substituent, rearrangement (resonance) in structure **II** is followed by deprotonation, then the benzene ring restores its aromaticity. In this mechanism, Structure **II** may give rise to three resonating structures with different environments.

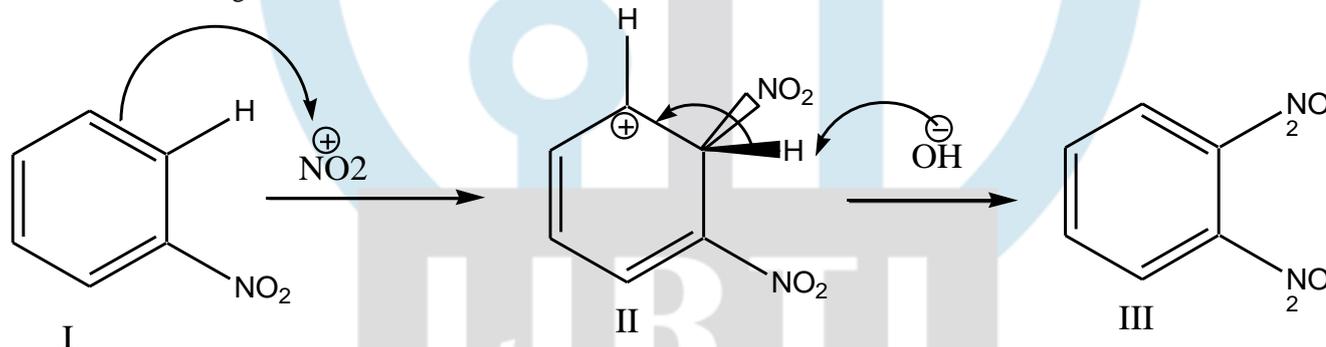


Figure-2. Mechanism-B showing the nitration at the ortho position and the deprotonation step.

Table-II. Energy calculated for each structure of mechanism B, total energy in hartrees and the relative energy in Kcal/mol.

Structure	AM1	RE	AM1 OPT	RE	B3LYP	RE
B-I	60	0	62	0	401814	0
B-II	384	324	258	196	402286	472
B-III	141	81	97	35	402194	330

Mechanism-C: This mechanism involves the attack at the meta-position to the substituent followed by 1,2- shift of the attacking electrophile (NO_2^+). The direction of the migration is from the meta-position to the ortho-position as shown in figure-3. Deprotonation finally gives back the aromaticity to the benzene ring. The migrating abilities of the incoming nitro group is very helpful for understanding the most probable mechanistic pathways. Mechanism C is nothing but the inclusion of mechanism A and B as well as transition state as a single mechanistic pathway.

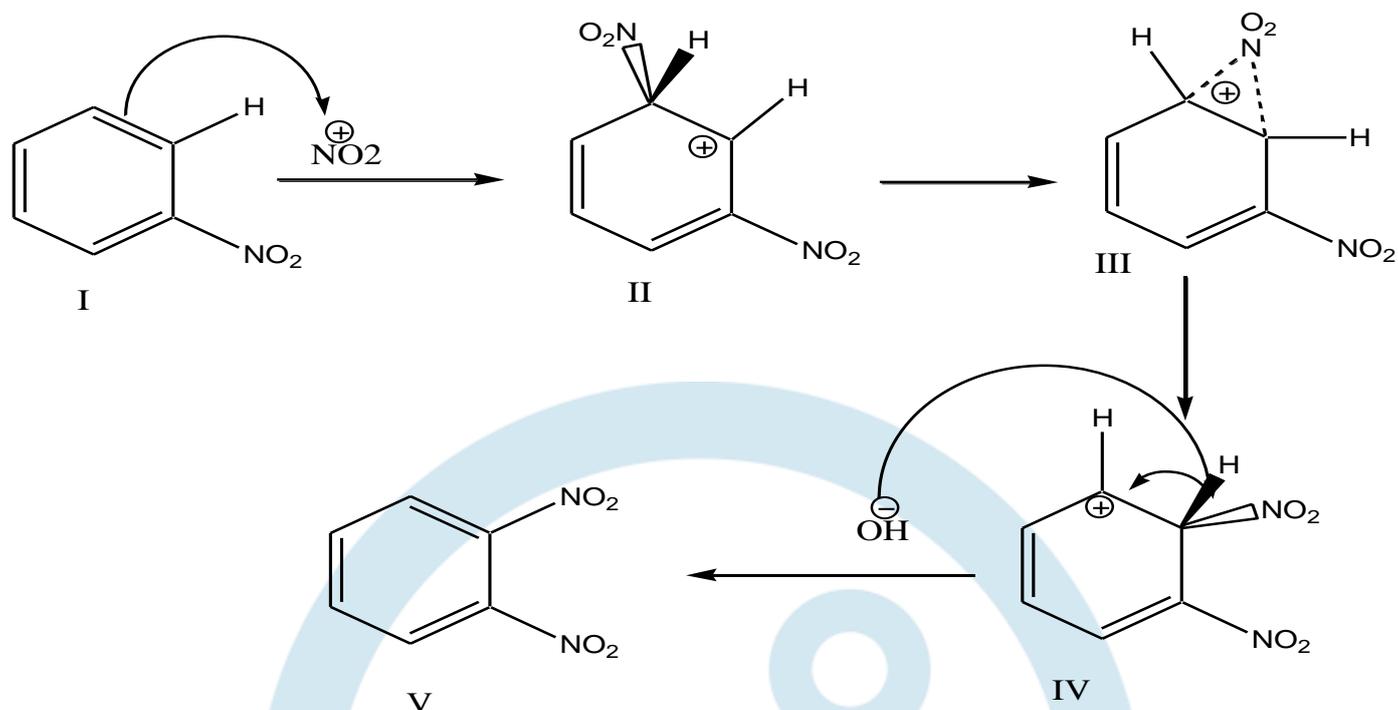


Figure-3. Mechanism-C showing the nitration of nitrobenzene initially at the meta-position and 1,2-shift of the incoming group via a transition state and the deprotonation step.

Table-III. Energy calculated for each structure of **mechanism C** and Activation energy for structure-II to III (*Ea-1*) and activation energy for structure-IV to III (*Ea-2*), total energy in hartrees and the relative energy in Kcal/mol.

Structure	AM1	RE	AM1 OPT	RE AM1 OPT	B3LYP	RE B3LYP	<i>Ea-1</i> (Kcal/mol) II→III	<i>Ea-2</i> (Kcal/mol) IV→III
C-I	60	0	62	0	401814	0	13	12
C-II	380.8	320.8	257	195	402283	469		
C-III			280	218	402298	484		
C-IV	384	324	258	196	402286	472		
C-V	141	81	97	35	402194	330		

Ea-1 gives the energy required for Structure –II(C-II) to climb up the peak of Transition state (C-III). The quantity of this energy determines the ease with which Structure-II(C-II) can be converted into structure-IV(C-IV). More the value of this energy more will be the energy required to get converted into structure-IV(C-IV). In the same way **Ea-2** describes the feasibility of conversion of structure-IV(C-IV) to structure-II(C-II).

As shown in the table, since structure-II(C-II) has energy lower than Structure-IV(C-IV), Ortho-substitution at the intermediate is supposed to increase the energy of the ring system to a greater extent than that of meta-substitution. Comparing structure A-III and B-III, energy calculated by different methods revealed that A-III has lower energy than B-III in all calculations. This is an indication of the more stability of molecule where the substitution is done at the meta-position than at the ortho-position when the substituent is an electron withdrawing group.

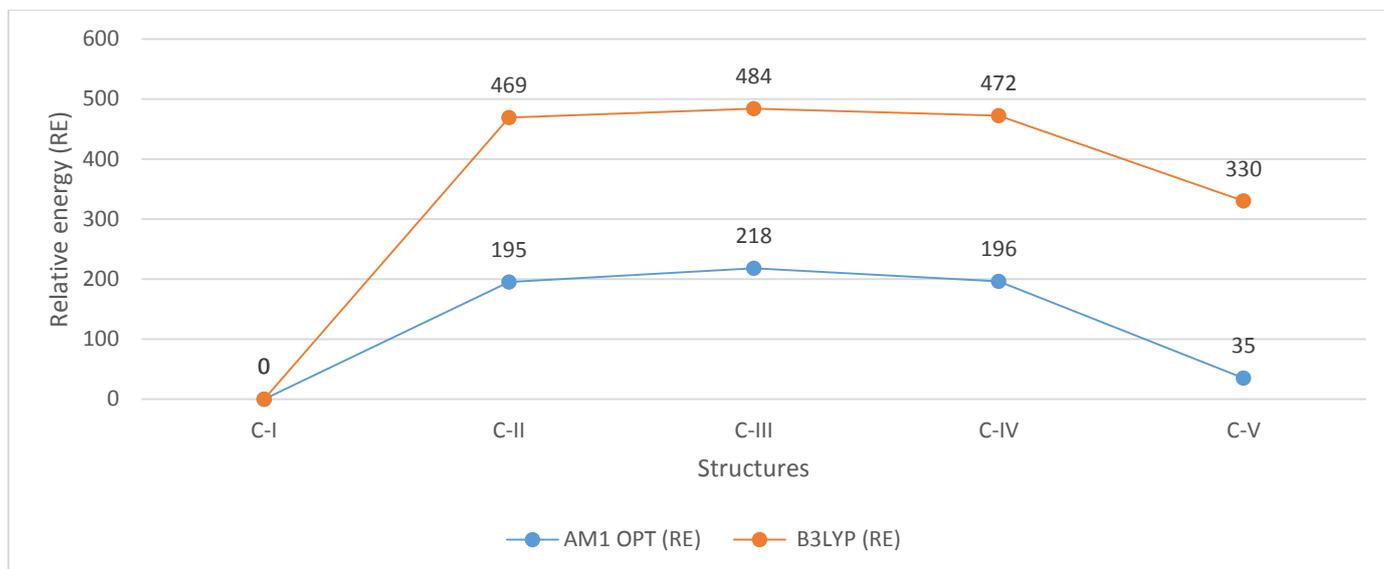


Figure-4 : Graph showing relative energy of different structures (from AM1 OPT and B3LYP calculation)

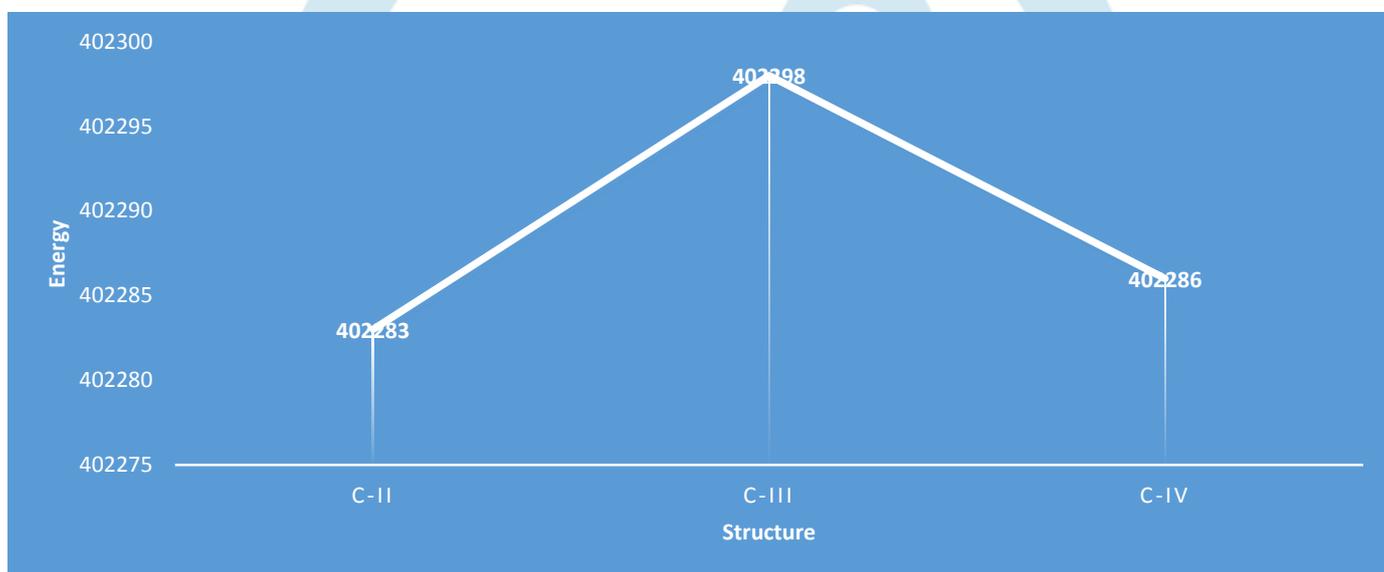


Figure-5: Graph showing the energy of structure II, III and IV. The differences in energy of C-II and C-III is Ea-1 and the differences in energy of C-IV and C-III is Ea-2.

Comparison of ortho and meta-position:

For each mechanism, structure-I is nitrobenzene. Therefore, the energy calculated was same for all mechanistic pathway. In mechanism C all the structures in mechanism A and B as well as structure C-III (Transition state) were included. In all calculations, structure B-II or C-IV has higher energy than structure A-II or C-II. It is attributed to the steric hindrance between two nitro groups which is more in structure B-II than that in structure A-II and possible localization of positive center at the carbon adjacent to nitro group. Since nitro group is an electron withdrawing group, creation of positive center adjacent to it will destabilize the intermediate. In addition to this, the nitro group deactivate the benzene ring by pulling electron cloud toward itself thus making the ring less facile for the attack of electrophilic reagent this effect is more pronounced at the ortho-position.

Structure A-III has less energy compared to B-III, the reason seems to lie upon the meta-directing property of nitro group by reason of its electron withdrawing effect and steric hindrance between two nitro groups located at the adjacent carbon atoms.

If we compare the activation energy of C-II and C-IV for climbing up transition state C-III, activation energy of C-II (Ea-1) is greater than C-IV (Ea-2), this implies that it is more easy to transform C-IV to C-II through transition state than from C-II to C-IV i.e. More energy will be required for transition from C-II to C-IV. On the other hand 1,2- shift from ortho to meta is easier than the reversed 1,2-shift if the substituent already present is an electron withdrawing group.

4. Conclusion:

From the theoretical study of aromatic electrophilic substitution reaction in the gaseous phase, The energy calculated for different structures in the mechanism and activation energy for 1,2-shift in ortho-meta transition reveals that meta substitution is more easier than that of ortho substitution if the substituent already present in the ring is an electron withdrawing group.

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