Theoretical Analysis of Electrophilic Substitution Reaction Based on Nitration of Toluene and Nitrobenzene in the Gas Phase

Joseph Lianbuanga[1*], Lijumon Lalremsanga[2]
[1] Research Scholar,Department of chemistry, Mizoram University, Pin-796704
[2]Department of Chemistry, Champhai College.

Abstract: The approach of this theoretical work is to study competitive mechanistic pathways in electrophilic substitution reaction to the substituted benzene. Where the substituents are nitro group and methyl group, the nucleophilic agent used is nitronium ion in both the cases. Three mechanistic pathways were proposed for each case, the first step of each of the three mechanisms involves nitration of the substituted benzene. In case of Nitrobenzene, the substituent, NO_2 group is electron withdrawing group and thus is likely to retard substitution reaction. But in case where the substituent is CH_3 group, (electron donating group) electrophilic substitution reaction is supposed to increase. All these calculations are done at the level of AM1 and density functional theory.

Keywords: Nitration, nitrobenzene, toluene, AM1, DFT

1. INTRODUCTION

Electrophilic aromatic substitution or EAS is an organic reaction in which an atom, usually hydrogen, appended to an aromatic system is replaced by an electrophile. The most important reactions of this type that take place are aromatic nitration[6], aromatic halogenation, aromatic sulfonation, acylation and alkylating Friedel-Crafts reactions [3]. Electrophiles may attack aromatic rings with functional groups. Performing an electrophilic substitution on an already substituted benzene compound raises the problem of regioselectivity. In case of a monosubstituted benzene, there are 4 different reactive positions. The ring carbon atom bearing the substituent is position 1 or ipso, the next ring atom is position 2 or ortho, position 3 is meta and position 4 is Para. Positions 5 and 6 are respectively equal to 3 and 2. In case where the substituent is electron donating group the attack at the ortho-position or Para-position are favorable. But if the substituent is electron withdrawing group Meta position will be the reactive centre.

Substituents can generally be divided into two classes regarding electrophilic substitution: activating and deactivating towards the aromatic ring. Activating substituents or 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 and thus decrease the reaction rate. They do so by withdrawing electron density from the aromatic ring, though the positions most affected are again the ortho and para ones. This means that the most reactive positions (or, least unreactive) are the meta ones (atoms 3 and 5). Examples of deactivated aromatic rings are nitrobenzene, benzaldehyde and trifluoromethylbenzene. The deactivation of the aromatic system also means that generally harsher conditions are required to drive the reaction to completion. An example of this is the nitration of toluene during the production of trinitrotoluene (TNT) [1].

In the first step of the reaction mechanism, the electron-rich aromatic ring which in the simplest case is benzene attacks the electrophile. This leads to the formation of a positively-charged cyclohexadienyl cation, also known as an arenium ion [2]. 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 Lewis base donates electrons to the hydrogen atom at the point of electrophilic attack, and the electrons shared by the hydrogen return to the system, restoring aromaticity [4]. An electrophilic substitution reaction on benzene does not always result in monosubstitution. While electrophilic substituents usually withdraw electrons from the aromatic ring and thus deactivate it against further reaction, a sufficiently strong electrophile can perform a second or even a third substitution. This is especially the case with the use of catalysts.

2. METHODOLOGY

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 was used to calculate the gradient-corrected electron density

function, geometries, energies and frequencies of different structure obtained in the mechanisms studied here. 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 saddle point or transition state .Once located, the transition state was verified, which yield only imaginary negative frequency. 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, as well as for calculating the enthalpy changes for each successive step in the reaction [7].

The approach of this theoretical work is to study different possible mechanistic pathways in aromatic nucleophilic substitution reaction. The study of those different reactions were based on the energy involved due to steric interaction, angle strain, geometries, frequency, etc. Once the energy for each of the pathways were calculated , the most probable mechanistic pathway can be predicted .In this approach the effect of electron donating and electron withdrawing power of compounds were also included as a factor of rate of reaction.

Six mechanistic pathways were proposed and each mechanism was studied by the application of scientific computational program [5]. The availability of such programs has made it possible to calculate quantities such as molecular energies and structures, bond energies, dipole moments, vibrational frequencies, thermochemical properties, and (rare and difficult) reaction pathways, which otherwise may find complications in experimental studies.

3. RESULT AND DISCUSSION

In electrophilic substitution reaction, the benzene ring acts as an electron source. The reaction conditions employed are designed to generate an electrophilic species. Once formed, the electrophile reacts with an arene, for benzene e.g., the structure of the ionic intermediate after attack by electrophile is a resonance hybrid of three resonance contributing structures which can be represented by a single structure showing the delocalization charge. This delocalized non-aromatic carbocation is termed as an arenium ion, Or often a sigma complex, since the electrophile is joined to the benzene via a new sigma bond. The sigma complex is not aromatic, however, because the sp3 hybrid carbon atom interrupts the ring of p-orbital, the nature of electrophilic attack thus is highly endothermic. The sigma complex, consequently regains aromaticity by the loss of proton on the tetrahedral carbon atom. 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 calculate with respect to the first structure for all the mechanisms studied. All values taken into consideration for our study here are taken from the DFT calculations.

3.2 Nitration of 1-Nitrobenzene

3.2.1 Mechanism IA:

This mechanism involves the attack of nitro group by the electron in the benzene ring at the meta-position as portrayed in Figure 2. Subsequently structure II loses its aromaticity, which is again regained by deprotonation in structure III. This deprotonation process being coerced by the electron-deficient carbocation center in the ring. Resonance in Structure II may evolve two possible carbocation centers with two different environments - in the ortho position between the two nitro groups and the para positions next to the substituted incoming nitro group - which are not considered in our study here due to time constraint, which may otherwise give a much clearer overview of the whole mechanism.

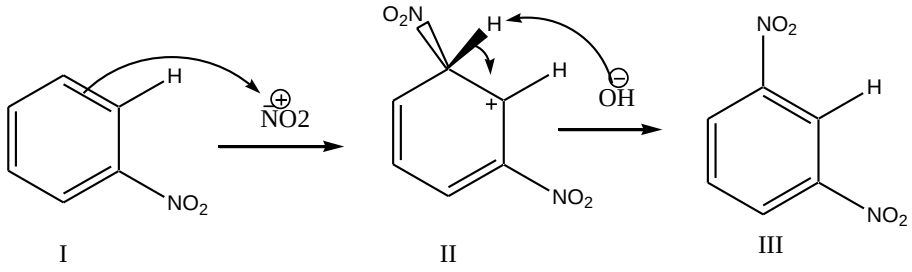

Figure 1. Mechanism IA showing nitration, and deprotonating steps.

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

3.2.2 Mechanism IIA

As shown in Figure 3, this second mechanism the attack occurs at the ortho-position to the substituent, rearrangement (resonance) in structure-II is followed by deprotonation, and then the benzene ring restores its aromaticity again to harbor the ortho substitution. In this mechanism too, resonance in Structure II may evolve two possible carbocationic centers with two different environments - in the Meta position next to the substituted incoming nitro group and in the ipso position. Further study may give a much clearer understanding of the whole mechanism and the charge distributions for a preferred and plausible mechanistic pathway.

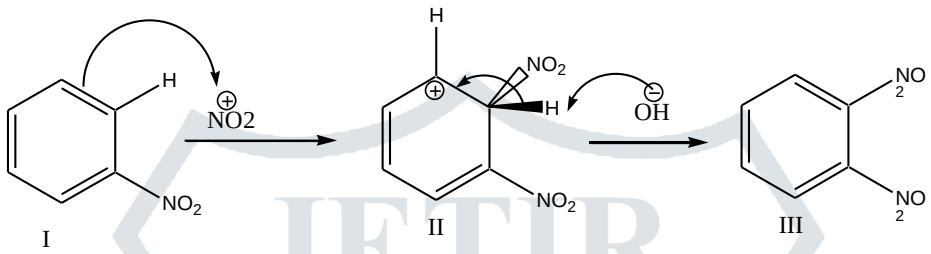

Figure 2. Mechanism IIA showing the nitration, and the deprotonation steps.

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

Structure	AM1	RE	AM1 OPT	RE	B3LYP	RE
I	60	0	62	0	401814	0
II	380.8	380	258	196	402283	469
III	141	81	97	35	402194	330

3.2.3 Mechanism IIIA

The first step of this mechanism is similar to that of Mechanism IA with an attack at the ortho position. The NO_2 undergo a 1,2-shift to form structure IV via a transition state labeled as structure III. The direction of the migration is from the meta-position to the ortho-position. Deprotonation finally gives back the aromaticity to the benzene ring. The migration possibilities due to resonances and shifting of the electron deficient center in the ring and similarly the deprotonation possibilities for the same reason may be a helpful contrivance in rationalizing the nature of such mechanisms.

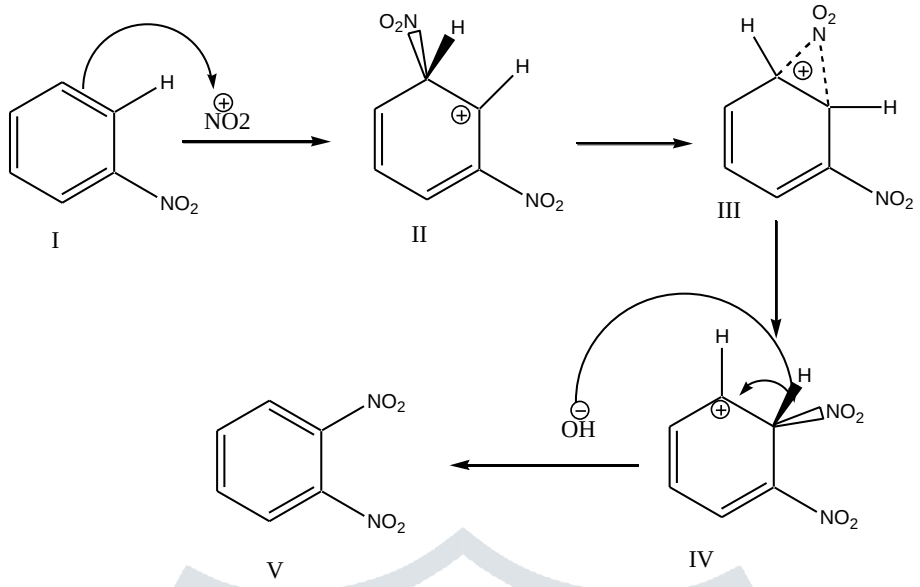

Figure 3. Mechanism IIIA showing the nitration, 1,2-shift via a transition state and the deprotonation step.

TABLE III. Energy calculated for each structure of **mechanism IIIA**, total energy in hartrees and the relative energy in Kcal/mol.

Structure	AM1	RE	AM1 OPT	RE	B3LYP	RE	Ea (Kcal.mol)	ΔH (Kcal.mol)
I	60	0	62	0	401814	0		
II	384	320	257	195	402286	472		
III			280	218	402298	484	12	3
IV	380.8	380	258	196	402283	469		
V	141	81	97	35	402194	330		

3.3 Nitration of Toluene.

Methyl group is an electron donating species. So it is expected to accelerate electrophilic substitution reaction in the benzene ring, different mechanistic pathways are given below;

3.3.1 Mechanism IB

The first step of the mechanism is similar to that is in mechanism IA. But here, the presence of activating group facilitates the electron at the meta position to attack electrophile, on account of the electron donating capacity of the substituent this reaction is likely to occur faster than mechanism IA. The attack at the Meta position leads to the formation of arenium ion which is followed by deprotonation from meta positon, deprotonation is persuaded by the positive charge created at the ortho position this is then followed product formation.

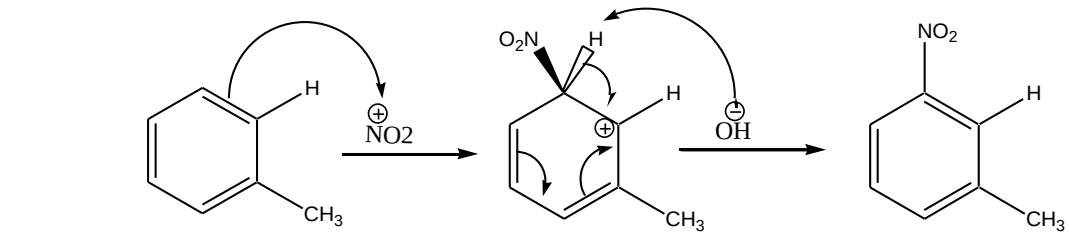

Figure 4. Mechanism IB showing the nitration, and the deprotonation steps.

TABLE IV. Energy calculated for each structure in mechanism IB, total energy in hartrees and the relative energy in Kcal/mol.

Structure	AM1	RE	AM1 OPT	RE	B3LYP	RE
I	32	0	51	0	298227	0
II	325	293	211	160	298725	498
IV	97	65	76	25	298622	395

3.3.2 Mechanism IIB

The attack of the π-electrons to the electrophile is aided by the substituent present at the ortho- position to the incoming group. The first step begins with the attack of the electrophile by the π-electron from the ortho position. The arenium ion formed as a result of first step bears positive charge at the meta-position. The positive charge formed here interacts with the substituent with negligible amount and can be ignored. But it is influenced by only one electron withdrawing group , here deprotonation occurs from the ortho position which is then followed by product formation

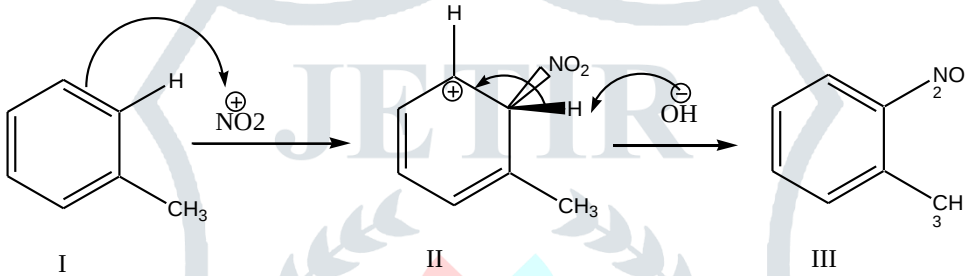

Figure 5. Mechanism IIB showing the nitration, and the deprotonation steps.

TABLE V. Energy calculated for each structure of mechanism IIB, total energy in hartrees and the relative energy in Kcal/mol.

NAME	AM1	RE	AM1 OPT	RE	B3LYP	RE
I	32	0	51	0	298227	0
II	312	280	221	170	298719	492
IV	98	66	77	26	298619	392

3.3.3 Mechanism IIIB

The first step of this mechanism is similar to that of Mechanism IIB.1,2 Shift happens when NO_2 undergoes transition from meta to ortho position. The reason why this happens is attributed to the stability of positive centre created at the meta position than in ortho position

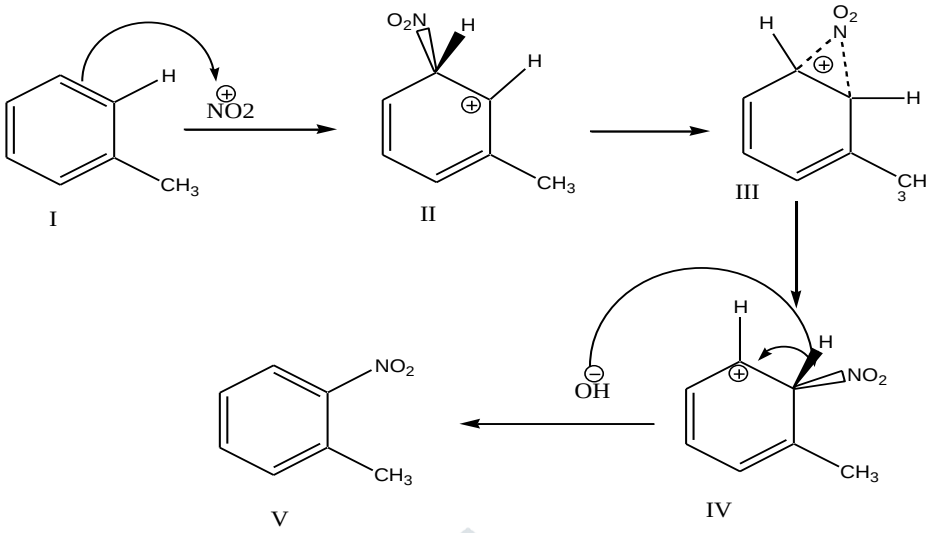

Figure 6. Mechanism IIIB showing the nitration, 1,2-shift via a transition state and the deprotonation step.

TABLE IIIB. Energy calculated for each structure of mechanism IIIB, total energy in hartrees and the relative energy in Kcal/mol.

Structure	AM1	RE	AM1 OPT	RE	B3LYP	RE	Ea (Kcal.mol)	ΔH (Kcal.mol)
I	32	0	51	0	298227	0		
II	325	293	224	173	298725	498		
III			279	228	298734	507	9	6
IV	312	280	221	170	298719	492		
V	97	65	76	25	298619	392		

3.4 Comparision of Ortho and Para position

In the first mechanism IA, our study concern with the electrophilic attack at the meta-position to the electron withdrawing substituent NO_2 creating positive charge at the ortho-position. This position is under the influence of two electrons withdrawing groups present adjacent to it, and thus making the ring very unstable. But in the second mechanism (IIA), nitration takes place at the ortho-position and the positive charge is created at the meta-position where the influenced by the substituent nitro group is reduced and the stability is more as compared to the first mechanism. This explanation can be attributed to the energy calculated where the nitration energy for mechanisms IA & IIA are 472 kcal/mol and 469 kcal/mol, respectively, a difference of 3 kcal/mol in favour of Mechanism IIA for the nitration step.

The nitration energy in the monosubstituted benzene is very high with the value of 195Kcal/mol(semi-emperical)and 427 Kcal/mol(DFT). Because, as the nitronium ion is attacked by the pi-elecrton of the the benzene ring, very unstable arenium ion is created and the benzene ring loses its aromaticity and moreover the steric interaction between the entering group and the substituent is also very large. In order to overcome all these energy large amount of energy is required to ensure reaction completion. In mechanism IA, deprotonation occurs from meta-position where the entering group is bonded, this is because, the positive charge developed at the ortho-position is to be neutralized by the adjacent electron pair and thus the hydroxyl ion deprotonates from this position. But in mechanism IIA deprotonation is from ortho-position in order to neutralize the positive charge developed at the Para-position.

3.5 Comparison of the two substituents for activation energy and heat of formation:

3.5.1 Mechanism IIIA

From figure 3, the activation energy is 12 Kcal/mol and the heat of formation is 3 Kcal/mol. For its high activation energy

comparing to its heat of formation, this reaction is endothermic and can only be attained by supplying large amount of energy. This high activation energy is due to the presence of deactivating nitro group.

3.5.2 Mechanism IIIB

From figure 6, The activation energy is 9Kcal/mol and the heat of formation is 6Kcal/mol. The activation energy of this reaction is less as compared to that of mechanism IIIA, and the heat of formation is more than that of mechanism IIIA. These imply that, though mechanismIIIB is endothermic in nature, it is more feasible than mechanism IIIA, the reason this is the presence of activating (electron donating) group in the benzene ring.

3.6 Comparition of two different substituents for the rate of substitution:

The substitution reaction depends upon the nature of substituent present in the benzene ring. Electron withdrawing group deactivates pi-electrons towards electrophilic substitution .In case where nitro group is the substituent, it pulls electron cloud towards itself and thus the benzene ring becomes electron deficient for electrophilic attack and thus slows down electrophilic substitution reaction. Deprotonation is fast if the substituent is nitro group.

But if the substituent is methyl group, electron cloud is pushed towards the benzene ring and thus making the benzene ring electron sufficient for electrophilic substitution. Thus methyl group or electron donating groups are known as activating groups.

3.7 Ea and ΔH as factors for feasibility of reaction:

The Ea for mechanism IIIA is 12 Kcal/mol. whereas it is 9Kcal/mol in mechanism IIIB .From their activation energy, Mechanism IIIB is found to be more feasible reaction than Mechanism IIIA. From the data, we can know that the reaction is more feasible when the substituent has +I effect (methyl group) and the reaction is less feasible when the substituent has –I effect (nitro group).

4. CONCLUSION

From the above results and discussion, the energy involved in the mechanistic pathways of Mech-IA and Mech-IB were found to be more favorable than the mechanistic pathways of Mech-IIA and Mech-IIB .Thus we can concluded that the reactivity of ortho-position is more comparing to that in meta-position, because in mechanism of Mech-IA and Mech-IB, the positive charge created at the ortho position is under the influence of two strongly electron withdrawing groups this further causes the instability of the benzene ring (arenium ion). But in mechanism of Mech-IIA and Mech-IIB, the positive charge developed at the meta-position is under the influence of only one electron withdrawing group and thus making the ring less unstable. Moreover, from the resonance structure, we can find that the electron cloud is more in the ortho-position than that in the meta-position for electrophilic attack and thus is the plausible position for electrophilic attack.

In mechanism IIIA electron withdrawing (nitro) group is present as the substituent, this group withdraws electron cloud towards itself and making the ring electron deficient for electrophilic attack, .Whereas in Mechanism-IIIB electron donating group (methyl) present in the ring donates electron clouds towards the ring and thus making the ring electron sufficient for electrophilic attack .Thus we can concluded that the electrophilic substitution reaction is more feasible when the substituent is electron donating group than when it is electron withdrawing group.

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