

## COMPUTATIONAL STUDY OF CONCERTED REACTION PATHWAYS FOR N-ALKYLANILINE TRANSFORMATION TO ANILINE IN ACID MEDIA AND UNDER GAS PHASE

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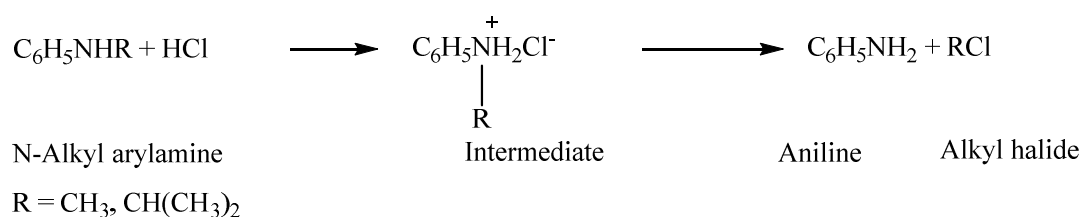
### ABSTRACT

Experimentally the transformation of N-alkylaniline to aniline is assumed to proceed by S<sub>N</sub>2 reaction pathway. New concerted reaction pathway was proposed. These concerted reaction pathways were studied computationally and compared using different alkyl substituents (methyl and isopropyl). The computational calculation was carried out with Density Functional Theory using B3LYP (Becke-style 3-Parameter Density Functional Theory, that use Lee-Yang-Parr correlation functional) and 6-311++G (d, p) basis set. The reaction pathways were followed and verified with Intrinsic Reaction Coordinate (IRC). It was found that, in accordance with the experimental assumption, S<sub>N</sub>2 reaction pathway was the choice of the transformation.

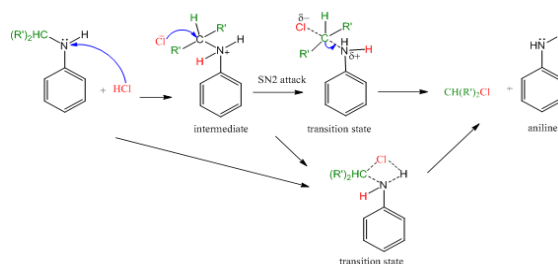
**KEYWORDS:** Aniline, Concerted Reaction Mechanism, Density Functional Theory, S<sub>N</sub>2 Transition State, Substituents Effect

### INTRODUCTION

The N-alkylarylamine(alkyl = methyl and isopropyl) react with hydrochloric acid to form the phenylalkyl ammonium chloride,<sup>[1]</sup> which then proceed via S<sub>N</sub>2 reaction<sup>[2]</sup> to give the product (Figure 1). New concerted reaction pathway was proposed. These concerted reaction pathways were studied and compared using different alkyl substituents. These conversion were computationally studied using Gaussian software. The calculation was carried out with Density Functional Theory using B3LYP (Becke-style 3-Parameter Density Functional Theory, that use Lee-Yang-Parr correlation functional) and 6-311++G (d, p) basis set. The computational investigation of the reaction mechanism was done with different alkyl substituents to follow the reaction path by Intrinsic Reaction Coordinate (IRC). The enthalpy of the reaction, free energy of the reaction, activation energies and rate of the reactions were calculated.



Proposed Mechanism (R' = H, CH<sub>3</sub>)



**Figure 1: Proposed Reaction Pathways for the Concerted Transformation of N-Alkylphenylamine to Aniline**

## COMPUTATIONAL PROCEDURE AND METHODOLOGY

All the electronic structure calculations are carried out using the Gaussian 09W, Revision A.02, program package [3]. In this investigation the geometrical optimization and harmonic vibrational frequencies of the reactants, complexes, transition states and the products are calculated under gas phase using the Density Functional Theory (DFT) with B3LYP three-parameter hybrid functional proposed by Becke [4]. The B3LYP functional comprises an exchange-correlation functional that mixes the nonlocal Fock exchange with the gradient-corrected form of Becke [5] and adds the correlation functional proposed by Lee et al. [6]. Unrestricted calculations are needed for processes such as bond dissociation which require the separation of an electron pair [7]. Otto has demonstrated that diffuse functions are necessary for describing the weak bond interaction [8]. Therefore, for all calculation u6-311++G (d, p) basis set is used. At the same level of theory the minimum energy path (MEP) is obtained by Intrinsic Reaction Coordinate (IRC) theory [9,10] from the transition state to the corresponding reactants and products respectively. The reactants and the products possess all real frequencies, whereas transition states possess one and only one imaginary frequency. All the reactants (r), intermediates (int), transition states (ts) and products (p) from the IRC are optimized again at the same model chemistry. The bond length and angle are compared with the literatures [11, 12, 13].

The values of thermochemical property [14] like Heat of the reaction ( $\Delta_r H^0$ ), Gibbs free energy of the reaction ( $\Delta_r G^0$ ), Activation energy ( $\Delta^\ddagger G^0$ ) and the Rate of the reaction [ $k(T)$ ] for proposed reaction pathways were calculated at 298K and 1 atm pressure using the following equations:

$$\Delta_r H^0 = \Delta H_{\text{product}} - \Delta H_{\text{reactant}} \dots \dots (1)$$

$$\Delta_r G^0 = \Delta G_{\text{product}} - \Delta G_{\text{reactant}} \dots \dots (2)$$

$$\Delta^\ddagger G^0 = \Delta G_{\text{transition state}} - \Delta G_{\text{reactant}} \dots \dots (3)$$

Rate of the reaction [15] for both reaction pathways are calculated using the following equation

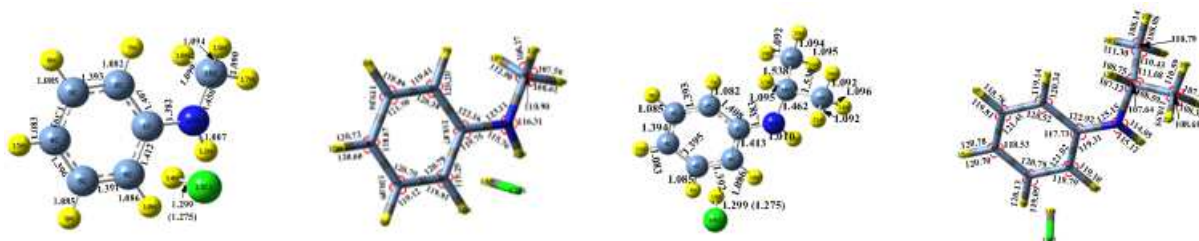
$$k(T) = \frac{k_B T}{h c^0} e^{-\Delta^\ddagger G^0 / RT} \dots \dots (4)$$

Where  $k_B$  = Boltzmann constant, T = temperature (default = 298.15), R = gas constant, h = Plank's constant,  $\Delta^\ddagger G^0$  = Gibbs free energy of activation,  $c^0$  = concentration and  $k(T)$  = reaction rate at temperature T.

## DISCUSSION AND RESULTS

The proposed reaction pathways are assumed to start from the same initial reactants, on acidification with hydrochloric acid is expected to pass through intermediate and form either  $S_N2$  transition state or cyclic transition state to give the final products. The investigation of the transformation of N-alkylphenylamine to aniline reaction mechanism is

started with finding the true transition state for both the proposed concerted pathways. Figure 2 show the optimized bond length (Angstroms, Å) and bond angle (degree) of the initial reactants *N*-methylaniline and *N*-isopropylaniline.



**Figure 2: The Bond Length in Angstroms (Å) and Bond Angle in Degree for the Initial Reactants (*N*-Methylaniline and *N*-Isopropylaniline), Parentheses in Hcl Bond Indicate the Experimental Bond Length**

The initial reactants are optimized together with HCl, therefore due to intermolecular interaction in gas phase they are expected to have bond length and bond angle values different from experimental crystalline solid values. Even then all the optimized structures have bond length and bond angle values very close to the experimental values, which indicate that the model chemistry used for computation is fit to carry out the theoretical investigation of these concerted reaction mechanisms and expected to give reliable calculation results.

### Main Proposed Mechanism of Reaction ( $S_N2$ Transition State Reaction Pathway)

The reaction sequence was generated by the protonation of the *N*-alkylphenylamine to give intermediate - *N*-alkylbenzenaminium chloride. This intermediate further undergo reaction via  $S_N2$  transition state to give the product – aniline and the haloalkane. The intrinsic reaction coordinate for both the *N*-methylbenzenaminium chloride and *N*-isopropylbenzenaminium chloride are shown in figure 3 and 4. Figure 5 show the bond length (Angstroms, Å) for the intermediates, transition states and the products from the intrinsic reaction coordinate of methyl and isopropyl substituent.

In *N*-methylbenzenaminium chloride (figure 5) the distance between the chloride ion ( $Cl_{18}$ ) and carbon ( $C_{14}$ ) of the methyl group is 2.787 Å (indicated by blue double head arrow) and between  $H_{19}$  (of HCl) and chloride ion is 4.770 Å. The chloride ion position itself in a favorable way for the formation of  $S_N2$  transition state, but result in high dipole moment and high optimized energy. In the transition state the distance between the methyl carbon ( $C_{14}$ ) and the chloride ( $Cl_{18}$ ) decreases to 2.576 Å and the distance between the nitrogen and the methyl carbon is increase from 1.586 Å to 1.769 Å. After forming the product, the chloromethane moves away from the nitrogen of the aniline by a distance 3.538 Å. For isopropyl substituent the distance between the  $C_{14}$  and nitrogen increases from 1.525 Å to 2.001 Å in the transition state. *N*-isopropylbenzenaminium chloride structure show that the chloride ion align itself along the plane of the aromatic ring which reduces the energy of its optimized structure and the dipole moment. In the product 2-chloropropane move away from N of the aniline by 3.627 Å.

Figure 6 show the bond angle (degree) for the intermediates, transition states and the products of methyl and isopropyl substituent. The transition state structure for methyl substituent show nearly 180° alignment along  $N_{12}$ ,  $C_4$  and  $Cl_{18}$ , due to electronic steric hindrance from the aromatic ring it is reduce to 178.39°. Figure 7 indicate experimental values of bond length and bond angle of aniline<sup>12, 13</sup>, chloromethane and hydrochloric acid<sup>11</sup>.

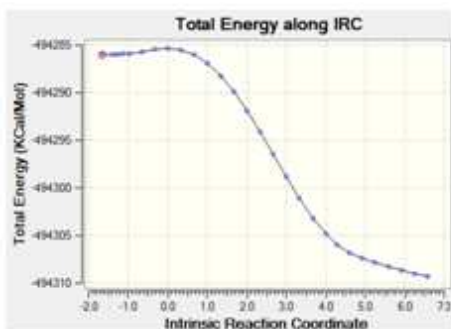


Figure 3: Intrinsic Reaction Coordinate for N-Methylbenzenaminium Chloride to Aniline and Chloromethane in  $S_N2$  Pathway

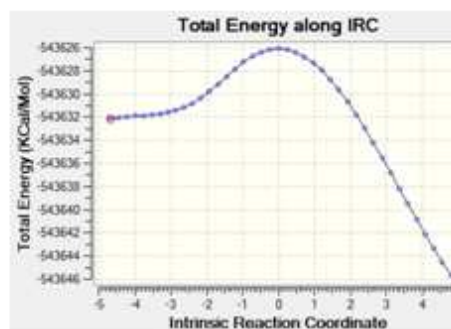
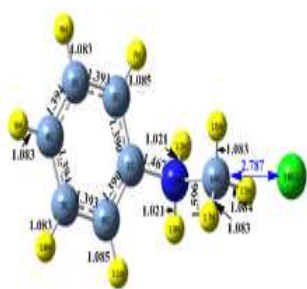
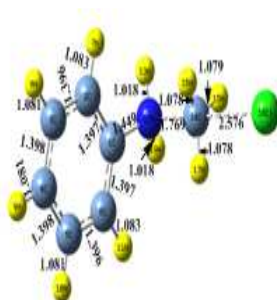


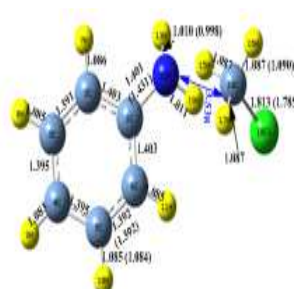
Figure 4: Intrinsic Reaction Coordinate for N-Isopropylbenzenaminium Chloride to Aniline and 2-Chloropropane in  $S_N2$  Pathway



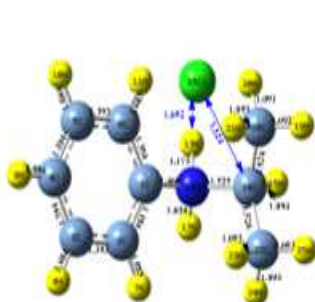
N-methylbenzenaminium chloride



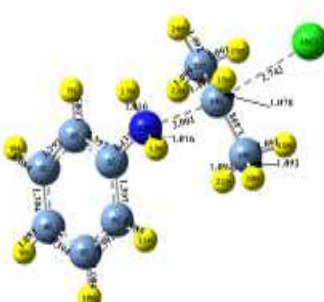
$S_N2$  Transition state (methyl)



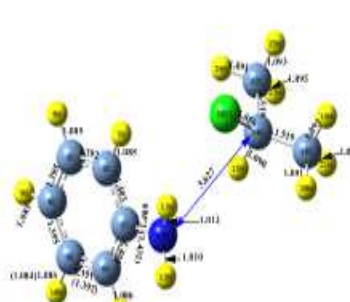
Aniline and chloromethane



N-isopropylbenzenaminium chloride

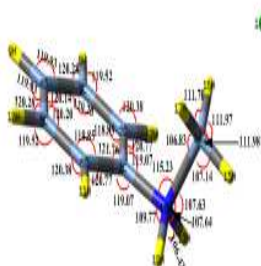


$S_N2$  Transition state (Isopropyl)

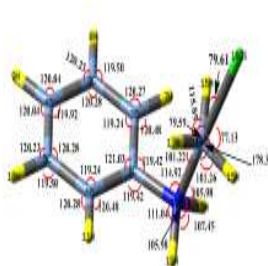


Aniline and 2-chloropropane

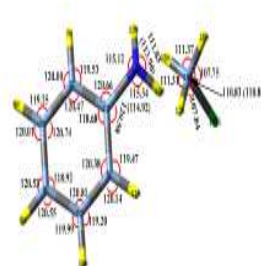
Figure 5: Bond Length in the Intrinsic Reaction Coordinate for Optimized Structure of Methyl and Isopropyl Substituent in  $S_N2$  Pathway Under Gas Phase, Values in the Parentheses Indicate the Experimental Bond Length Values of Crystalline Solid (Reference No. 11)

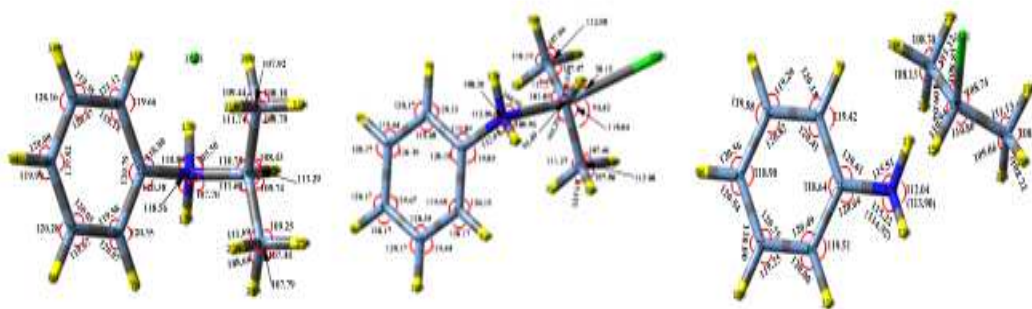


N-methylbenzenaminium chloride



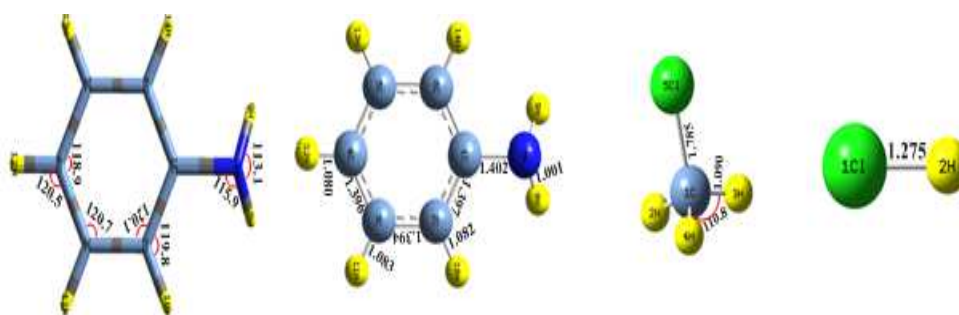
$S_N2$  Transition state (methyl) Aniline and chloromethane



N-isopropylbenzenaminium chloride  $S_N2$  Transition state (Isopropyl)

Aniline and 2-chloropropane

**Figure 6: Bond Angle of the Optimized Structures From the Intrinsic Reaction Coordinate of Methyl and Isopropyl Substituent in Gas Phase, Values in the Parentheses Indicate the Experimental Bond Angle Values of Crystalline Solid (Reference No11)**



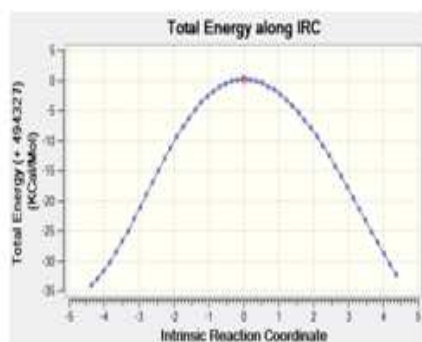
**Figure 7: Bond Length and Angle of Aniline from Reference No 12 and 13, Chloromethane and HCl from Reference No 11**

### New Proposed Mechanism of Reaction (Cyclic Transition State Reaction Pathway)

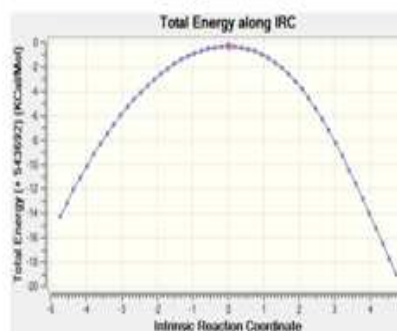
The new proposed pathway is expected to form the intermediate similar to  $S_N2$  reaction pathway then further form the transition state. However it was observed that the optimized structure from the calculation of intrinsic reaction coordinate of their respective cyclic transition state indicate only N-isopropylaniline form the intermediate N-isopropylbenzenaminium chloride, where N-methylaniline does not give the intermediate but proceed straight to the cyclic transition state. The seintermediates further undergo reaction via cyclic transition state to give their respective products. The intrinsic reaction coordinate via cyclic transition pathway for both the substituents are shown in figure 8 and 9. Figure 10 show the bond length (Angstroms, Å) for the reactants, intermediates, transition states and the products from the intrinsic reaction coordinate of methyl and isopropyl substituent. Similarly, Figure 11 show the bond angle (degree) for the intermediates, cyclic transition states and the products of methyl and isopropyl substituent. The distance between  $N_{12}$  (N-Methylaniline) and  $H_{18}$  (HCl) is 1.738 Å, which is close enough to form a bond and the HCl bond is elongated to 1.348 Å from 1.275 Å. The bond length of  $C_1$  and  $N_{12}$  is 1.422 Å while  $N_{12}$  and  $C_{14}$  is 1.468 Å. In the transition state there is a partial bond (1.015 Å) formation between  $N_{12}$  and  $H_{18}$ , HCl bond further elongate to 2.431 Å, the bond between  $N_{12}$  and  $C_{14}$  also extend further to 2.255 Å. There is new partial bond formation between  $C_{14}$  and  $Cl_{19}$  (2.572 Å).  $C_{14}$  of chloromethane move away from the  $N_{12}$  of aniline by 3.537 Å to give the optimized products.

For N-Isopropylaniline, it undergo protonation to give the intermediate, N-isopropylbenzenaminium chloride, then form the cyclic transition state to give the products. The bond length in the intermediate between  $C_1$  and  $N_{12}$  is 1.464 Å,  $N_{12}$  and  $H_{16}$  is 1.155 Å,  $H_{16}$  and  $Cl_{17}$  is 1.730 Å,  $N_{12}$  and  $C_{14}$  is 1.523 Å. The transition state show new partial bond

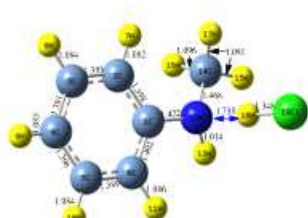
formation and elongation of the old bond, N<sub>12</sub> and C<sub>14</sub> is 2.620 Å, H<sub>16</sub> and Cl<sub>17</sub> is 2.087 Å, C<sub>14</sub> and Cl<sub>17</sub> is 2.990 Å. While C<sub>1</sub> and N<sub>12</sub> (1.399 Å), N<sub>12</sub> and H<sub>16</sub> (1.032 Å) begin to reduce to normal bond length.



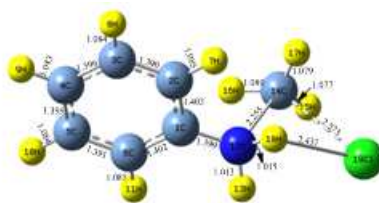
**Figure 8: Intrinsic Reaction Coordinate for N-Methylbenzenaminium Chloride to Aniline and Chloromethane in Cyclic Pathway**



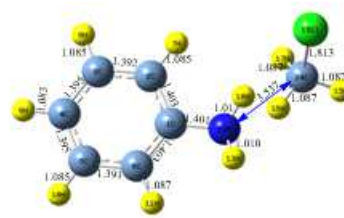
**Figure 9: Intrinsic Reaction Coordinate for N-Isopropylbenzenaminium Chloride to Aniline and 2-Chloropropane in Cyclic Pathway**



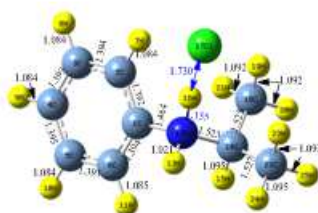
*N*-Methylaniline & HCl



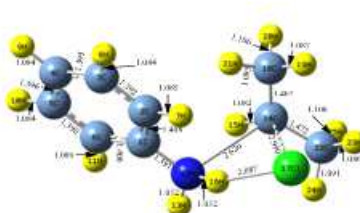
Cyclic Transition state



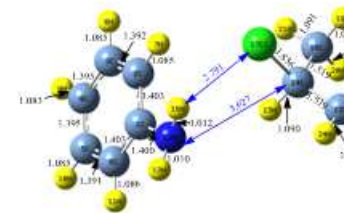
Aniline & Chloromethane



*N*-isopropylbenzenaminium chloride

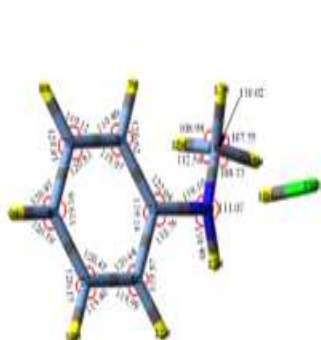


Cyclic Transition State

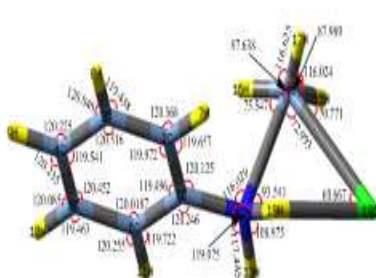


Aniline & 2-Chloropropane

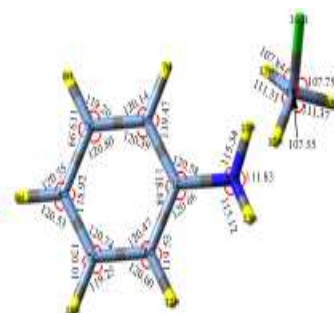
**Figure 10: Bond Length in Angstroms (Å) of Optimized Structures from the Intrinsic Reaction Coordinate for Methyl and Isopropyl Substituent in Cyclic Pathway Under Gas Phase. Blue Arrow in the Reactants Indicate the Distance Between the Reacting Species and in the Product it Indicate the Distance by Which They Move Away From Each Other**



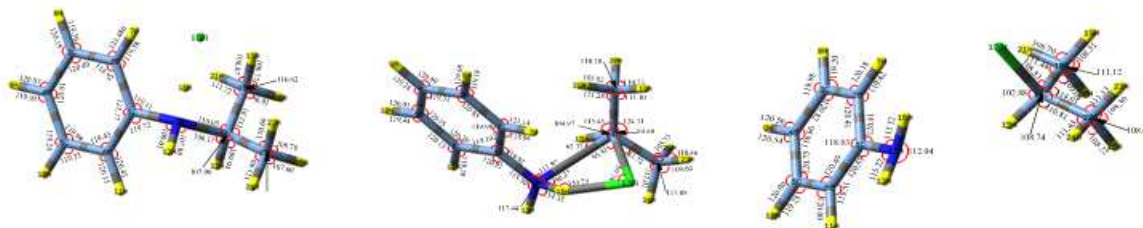
*N*-Methylaniline & HCl



Cyclic Transition State (Methyl)



Aniline & Chloromethane



*N*-isopropylbenzenaminium chloride Cyclic Transition State (Isopropyl) Aniline & 2-Chloropropane

**Figure 11: Bond Angle in Degree of the Optimized Structures from the Intrinsic Reaction Coordinate of Methyl and Isopropyl Substituent in Gas Phase**

### Comparison of Findings for Both the Concerted Reaction Pathways

The theoretical investigation of the two concerted reaction mechanism were compared. Table 1 illustrate the computational values of Internal thermal energy, ( $E_{tot}$ ), Constant volume heat capacity, ( $C_{tot}$ ), Entropy, ( $S_{tot}$ ) and Dipole moment (Debye) of methyl and isopropyl substituents in  $S_N2$  TS and Cyclic TS pathways. Table 2 show the calculated values of Enthalpy of the reaction ( $\Delta_r H^0$ ), Free Energy of the Reaction ( $\Delta_r G^0$ ), Activation Energy of the Reaction ( $\Delta^\ddagger G^0$ ) and Rate of the Reaction ( $k$ ) at 298K.

**Table 1: Internal Thermal Energy,  $E_{tot}$  (Kcal/Mol), Constant Volume Heat Capacity,  $C_{tot}$  (Cal/Mol-Kelvin), Entropy,  $S_{tot}$  (Cal/Mol-Kelvin) and Dipole Moment of Methyl and Isopropyl Substituents in  $S_N2$  TS and Cyclic TS Pathways**

Substituent	Reaction Pathway	Structure Name	$E_{tot}$	$C_{tot}$	$S_{tot}$	Dipole Moment
Methyl	$S_N2$ TS	N-Methylaniline&HCl	102.539	37.475	106.377	3.1965
		N-methylbenzenaminium chloride	105.690	34.646	101.606	16.8862
		Transition state	104.481	33.645	98.460	14.0530
		Aniline & Chloromethane	104.312	36.583	110.334	1.4912
	Cyclic TS	N-Methylaniline&HCl	102.988	34.546	99.857	4.0683
		Transition state	103.099	35.088	101.767	6.8046
Aniline & Chloromethane		104.313	36.582	110.440	1.4912	
Isopropyl	$S_N2$ TS	N-Isopropylaniline&HCl	139.364	47.859	119.608	3.2525
		N-isopropylbenzenaminium chloride	140.828	43.473	108.362	8.6149
		Transition state	140.834	44.857	112.434	13.1572
		Aniline & 2-Chloropropane	141.221	47.056	125.136	1.9445
	Cyclic TS	N-Isopropylaniline&HCl	139.364	47.859	119.608	3.2525
		N-isopropylbenzenaminium chloride	141.038	43.487	108.415	8.5619
		Transition state	139.102	45.813	112.185	7.5084
		Aniline & 2-Chloropropane	141.222	47.053	124.885	1.9422

**Table 2: Calculated Values of Enthalpy of the Reaction ( $\Delta_r h^0$ ), Free Energy of the Reaction ( $\Delta_r g^0$ ), Activation Energy of the Reaction ( $\Delta^\ddagger G^0$ ) and Rate of the Reaction ( $k$ ) At 298K**

Substituents	Reaction Pathway	$\Delta_r H^0$ kcal/mol	$\Delta_r G^0$ kcal/mol	$\Delta^\ddagger G^0$ kcal/mol	$k$ per sec
Methyl	$S_N2$ TS	0.362	-0.819	38.859	$1.90563 * 10^{41}$
	Cyclic TS	3.973	0.817	54.552	$6.08514 * 10^{52}$
Isopropyl	$S_N2$ TS	-2.265	-3.913	38.643	$1.32340 * 10^{41}$
	Cyclic TS	-2.264	-3.837	42.847	$1.59795 * 10^{44}$

Plot of potential energy surfaces of  $S_N2$  transition state and cyclic pathway for N-methylaniline and N-isopropylaniline to their respective products are shown in figure 12 and 13.

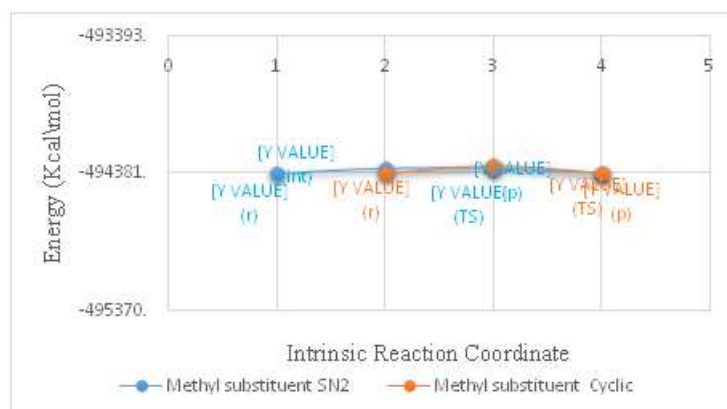


Figure 12: Potential Energy Surface Comparison for Methyl Substituent in  $S_N2$  and Cyclic Reaction Pathway

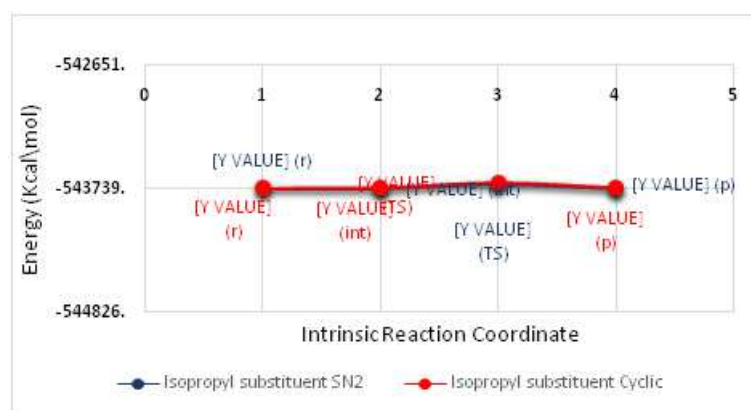


Figure 13: Potential Energy Surface Comparison for Isopropyl Substituent in  $S_N2$  and Cyclic Reaction Pathway

## CONCLUSIONS

In this work the reaction mechanism for the transformation of N-alkylaniline with acid to aniline under gas phase was explained from the computational chemistry point of view. The main goal was to prove that the reaction occurs through a mechanism that falls into a concerted mechanistic scheme. Due to the position of the chloride ion, the N-methylbenzenaminium chloride has a high dipole moment and undergoes the  $S_N2$  transition state easily. For cyclic transition state the N-methylaniline does not undergo N-methylbenzenaminium chloride (intermediate) formation. In N-isopropylaniline both the concerted transition states show N-isopropylbenzenaminium chloride (intermediate). From the calculation of the intrinsic reaction coordinate, activation energies and rate of the reactions in both the substituents confirm that the concerted mechanism can occur in the two proposed pathways and the  $S_N2$  concerted mechanistic pathway is more favored.

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