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Investigation of amine inversion dynamics in ortho and meta substituted anilines by G3XMP2 theory

Krishnan Chandrasekaran

Department of Chemistry, Vel Tech University, Chennai, India

ABSTRACT

G3XMP2 investigation of amine inversion dynamics of meta and ortho aniline have been studied extensively in this report. It reveals that ortho substituent decreases the inversion barrier by proximity electrical effects. Electronegative substituent at the ortho position forms strong intramolecular hydrogen bond with the amine group and promotes planar configuration. However, electron donating substituent increases the inversion barrier due to steric effects and causes non-planar configuration. Meta substituent alters the amine configuration based on the inductive effects. Electronegative substituents present in meta aniline derivative induces planar amine configuration by negative inductive effects.

Keywords: Amine, Inversion barrier, Planarity, Inductive effects, aniline

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INTRODUCTION

Amine inversion is of greater significance in chemical and biological interactions. The configuration of amino group influences the structure and molecular recognition process of nucleic acids.**[1]** Amino group in the nucleotides often interacts with the DNA bases and molecular systems during the biological process and accounts for structural modification.. Crystallographic database information have revealed that the amino group hydrogen atom can form strong out-of-plane hydrogen bond, so as the amine group nitrogen acts as weak hydrogen bond acceptor in the DNA base pair.**[2-4]** The out-of-plane hydrogen bond is related to the non-planarity of amino group in DNA bases. Besides, the earlier ab initio theoretical investigation conducted at 1990's arrived conclusion of non-planar amino group in DNA bases. **[5-6]** It is further authenticated by microwave studies, that the amino group of aniline is non planar and lies at an angle between 37° and 46º from the plane of phenyl ring.**[7-8]** Therefore the investigation of amino group structure by high level ab initio, DFT and MP2 level of calculation is inevitable to solve the subtle configuration of amine group. Moreover the investigation of amine inversion phenomenon will provide useful information of drug-receptor interaction, biological interactions and molecular recognition process. The present investigation addresses the ab initio and DFT structure analysis of amine group in ortho aniline and meta aniline derivatives. The salient feature of the ortho substituted aniline is the formation of intra molecular hydrogen bond with the hydrogen atom of the amine group. Aniline substituted with nitro, carboxyl and hydroxyl group deserves special attention, as these groups contain an oxygen atom that lies next to the hydrogen of aniline molecule, which has more probability to form an intramolecular hydrogen bond with the amine group. Since the ortho substituents are bound to the adjacent position of the side chain, various kinds of proximity effects, such as steric, proximity and electrical effects will play its contribution to the amino group and generally operates on the side chain functions **[9]**. Hydrogen bonding and other intramolecular interactions of ortho substituent plays a significant role on the structure of amine group and its inversion dynamics. **[10-11]**

MATERIALS AND METHODS

Computational Method

All the compounds were optimized using the DFT B3LYP/6-31G (2df, p) level of theory using the Gaussian 03 program.**[12]** The ortho and meta substituted prototype aniline molecules were optimized in both planar and non planar structures. No geometrical constraints were imposed to obtain the minimum energy structure of para and meta anilines. The non-planar configuration of aniline molecule is made by placing the nitrogen atom out of benzene plane ring; however, for the planar structure the amine group lies in the plane of phenyl ring. Frequency calculations and zero point energies were calculated using the B3LYP/6-31G (2df, p) level of theory and scaled by the 0.9854 factor. Single point energy calculations were made using QCISD(T)/6-31G(d), MP2/6-311g++(2df,2p) and HF/G3XL level of theory. Inversion barrier of ortho aniline and meta derivative anilines were calculated using the composite G3XMP2 theory and its details are available in the cited reference **[13]**.

RESULTS AND DISCUSSION

The effect of ortho substituent is expressed in terms of the proximity electrical and steric effects. Hydrogen bonding and other intramolecular interactions can be treated as electrostatic interactions. The steric hindrance is observed especially for the electron donating groups mainly imparted by the methyl group.

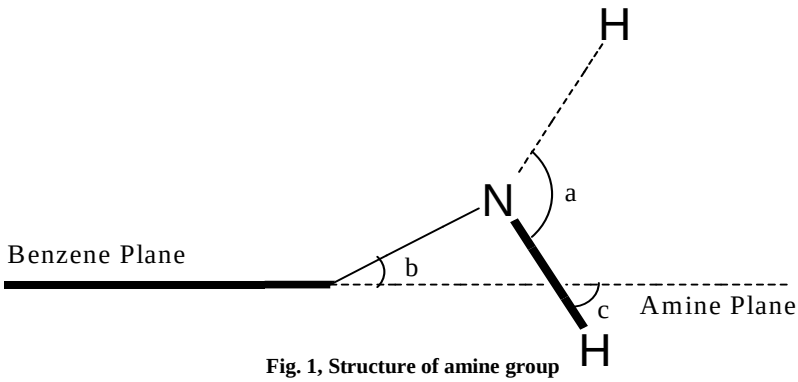

Fig. 1, Structure of amine group

Table I, shows the structural parameters of ortho substituted aniline. It is interesting to note that nitro and carboxyl group at the ortho position forms an interamolecular hydrogen bond with amine group.**[14]** This intramolecular hydrogen bond promotes the planarity of the amine by increasing electron delocalization of benzene ring. It is clear from **table I** that the electron withdrawing substituent favors planar amine structure by forming strong intramolecular hydrogen bond. However, electron donating substituents fails to form intramolecular hydrogen bond with the amine group and causes non-planar amine structure. The structure of amine group is shown in the **fig. 1** and it depicts that the nitrogen atom of the amino group is tilted from the ring plane and the two amino hydrogen atoms are deviated from the nitrogen plane. The inversion angle is denoted as "a", out of plane angle is denoted as "b" and tilt angle is denoted as 'c" of amine structure. Inversion angle is the vital structural parameter used to measure the pyramidalization of the amine group and pyramidilization of amine group is shown in **fig.2**. The asymmetric interaction between phenyl ring and amine nitrogen causes minor deviation of nitrogen atom from the ring plane and this displacement causes the non-planar structure of the amine group.

Effect of substituents on inversion barrier (Ortho aniline)

Electron withdrawing substituents such as cyano, nitro and aldehyde group forms strong intramolecular hydrogen bond with the amine group and promotes the planar configuration. The structure of ortho aniline is shown in the **fig. 3**. It is apparent from **table I** that the nitro, aldehyde and methoxy substituent drastically reduces the inversion barrier from 499.23 cm^{-1} to 34.65, 26.36 and 37.58 cm^{-1}. It indicates that the proximity electrical effects have substantial effect on inversion barrier. Besides, the electron withdrawing substituent increases the symmetric interaction between amine group and the phenyl ring, which in turn increases HNH bond angle and accounts for additional planarity of amine group.

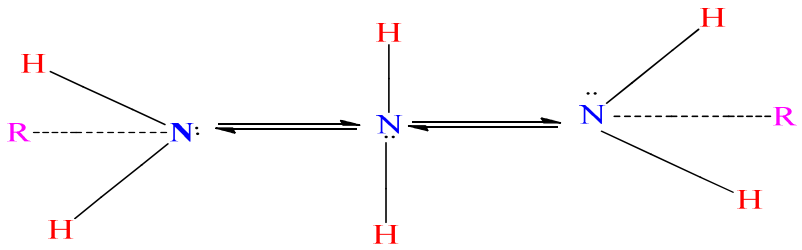

Fig. 2, Amine inversion process, R – is the phenyl ring

Cyano substituent at ortho position has significant effect on inversion barrier and it reduces the barrier from 499 cm^{-1} to 200 cm^{-1}, imparts planar configuration of amine group. Substituents such as chlorine and fluorine have mild effect on inversion barrier and hence its effects is trivial. However, chlorine forms strong intramolecular hydrogen bond and imparts planar configuration of amine due to higher electronegative inductive effect. In summary electronegative substituents decreases the inversion barrier by forming intramolecular hydrogen bond and thus causes planar configuration of amine group.

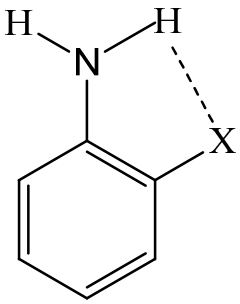

Fig. 3, Structure of ortho aniline, X – is the ortho substituent.

Electron donating substituent increases the inversion barrier and accounts for non-planar configuration. Methyl group at ortho position causes steric effect and fails to form strong intramolecular hydrogen bond; hence it increases the inversion barrier to 530 cm^{-1} and causes non-planar configuration of amine group. Inversion barrier of methyl group agrees well with the experimental value **[15]** of 558 cm^{-1}, this agreement authenticates the accuracy of G3XMP2 theory.

Table I

Serial No.	Ortho Substituents	Inversion barrier (cm^{-1})	H-N-H Bond angle ^{o}	d (C–N) Å	Inversion angle ^{o}	Tilt angle ^{o}	Out of plane angle ^{o}
1.	H	499	111.16	1.397	42.35	2.5	44.85
2.	-F	492	112.22	1.390	42.31	2.79	45.10
3.	-OH	497	112.08	1.350	12.32	2.26	14.60
4.	$-CH_3$	531	110.95	1.390	43.37	3.00	46.37
5.	-CN	201	114.58	1.390	42.93	2.65	45.58
6.	$-NO_2$	35	116.65	1.370	31.85	2.02	33.86
7.	-Cl	380	113.08	1.370	28.39	3.13	31.51
8.	-COOH	391	116.65	1.380	39.14	2.30	41.44
10.	-CHO	26	120.82	1.350	10.78	1.05	11.83
11.	$-NH_2$	1102	109.77	1.400	48.54	3.8	52.34
12.	$-OCH_3$	37	112.04	1.390	44.69	2.7	47.39

Table I illustrates that the methyl group attains higher tilt angle of 3^o due to high electron density around amine nitrogen produced by hyper conjugative effect and steric hindrance effect, thus it makes amine structure non-planar. Steric hindrance and hyperconjucative effect of methyl group decreases the HNH bond angle to 110^o and thus fails to form strong hydrogen bond. Amino group at the ortho position increases the inversion barrier two fold of aniline molecule to 1101 cm^{-1}. The massive increase in inversion barrier for amino group is due to the flow of enormous positive inductive effect and nucleophilic nature of amino group. The higher electron density around amine group decreases the C–N interaction by increasing the C–N bond length to 1.4Å and also decreases the HNH bond angle to 109^o, this structural alteration causes highly non-planar amine structure. It is apparent that electro-positive substituent due to their inherent positive inductive and hyperconjugative effect decreases the HNH bond angle and C–N interaction; so it favors non-planar configuration of amine structure.

Influence of substituents on inversion barrier (Meta aniline)

Meta substituents have moderate influence on the inversion barrier relative to ortho substituents. Generally meta substituents exert their effect purely by inductive effect and thus it lacks interaction with aromatic π system. Nitro and cyano group at the meta position decreases the inversion barrier to 372 cm^{-1} and 394 cm^{-1} by negative inductive effects and favors planar amine configuration. It increases the symmetric interaction between phenyl ring and amine nitrogen by decreasing C–N bond distance from 1.397Å to 1.38Å; so as it flattens the amine structure. Chlorine and fluorine substituents have little effect on the inversion barrier and it produces height of 447 cm^{-1} and 462 cm^{-1}; which is same as the aniline molecule. Hence its effect on the amine geometrical configuration is futile. Electron donating substituents enhances the electron density around amine nitrogen by positive inductive effect and causes the amine group to deviate from phenyl ring.

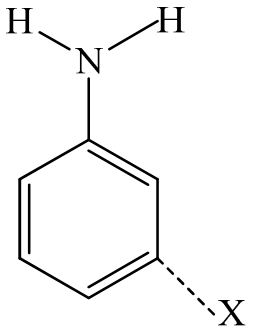

Fig. 4, Structure of meta aniline, x-is the meta substituent

Hydroxyl group at the meta position attains high inversion barrier of 654 cm^{-1}. It is known fact that hydroxyl group is electron donating substituent; thus it increases the electron density around amine nitrogen by positive inductive effect and subsequently favors the non-planar configuration of the amine group. The structure of meta substituted aniline is shown in the **fig. 4**. Similarly, the methyl group at meta position also promotes non-planar amine structure by increasing the inversion barrier to 534 cm^{-1} due to asymmetric interaction between nitrogen and phenyl ring and their inherent hyperconjugation. **Table II**, clearly illustrates that the amino group at meta position attains higher tilt angle of 2.57^o among all eleven substituents and causes high degree of non-planarity. In a nutshell the investigation concludes that electronegative substituents decreases the inversion barrier by inductive effects and favors planar amine structure. On the otherhand electron donating substituents increases the electron density around amine nitrogen by hyper conjugative effect and increases the inversion barrier, accounts for non-planar configuration.

Table II

Serial No.	Meta Substituents	Inversion barrier (cm^{-1})	H-N-H Bond angle ^{o}	d (C–N) Å	Inversion angle ^{o}	Tilt angle ^{o}	Out of plane angle ^{o}
1.	H	499.23	111.17	1.397	42.35	2.5	44.85
2.	-F	462.14	111.65	1.390	41.38	2.39	43.43
3.	-OH	372.39	112.29	1.380	38.89	2.37	41.26
4.	$-CH_3$	394.41	111.45	1.390	41.94	2.39	44.33
5.	-CN	447.26	111.13	1.390	42.68	2.29	44.97
6.	$-NO_2$	462.23	112.14	1.380	39.17	2.32	41.49
7.	-Cl	534.11	111.75	1.390	40.91	2.41	43.32
8.	-COOH	654.60	111.79	1.390	40.53	2.44	42.97
10.	-CHO	421.94	111.96	1.390	40.10	2.46	42.56
11.	$-NH_2$	546.00	110.94	1.390	43.22	2.57	45.79
12.	$-OCH_3$	540.74	111.08	1.390	42.90	2.54	45.44

CONCLUSION

G3XMP2 investigation of amine inversion dynamics by ortho and meta substituent concludes that the electron withdrawing substituent decreases the inversion barrier by strong electron delocalization and negative inductive effects; accounts for planar amine structure. Meanwhile electron donating substituents increases the inversion barrier by hyperconjugative effect and promotes non-planar amine structure. Ortho substituent forms strong intramolecular hydrogen with the amine group and imparts planar amine structure, whereas meta substitents exerts inductive effect and contributes to the planar amine structure. Steric effects and electrical effects played a central role in ortho substituents in promoting flat amine structure. The symmetric interaction between nitrogen atom and phenyl ring increases the HNH bond angle and causes planar configuration of ortho aniline derivatives. Meta aniline derivative experience negative inductive effect and promotes the planar amine structure. The G3XMP2 investigation of amine inversion dynamics provides useful information about the configuration of amine group in the phenyl ring. The calculated values agree well with the experimental data and therefore these findings will have greater

applications in biological interactions, protein folding, DNA base paring, drug design and molecular recognition process.

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