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Original Article

G3XMP2 INVERSION STUDIES OF HETEROAROMATIC AMINES, N-ANILINE AND N, N-ANILINE DERIVATIVES

KRISHNAN CHANDRASEKARAN

Vel Tech University, Chennai 600062, India.
Email: nuskrishnan@yahoo.com.sg

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ABSTRACT

Objective: Nitrogen inversion in aniline and hetero aromatic amines are contrary in nature and hence inversion dynamics of the above two compounds are investigated by G3XMP2 theory to determine the configuration of the amine group. Besides, the structure and dynamics of N-aniline and N,N-aniline derivatives are also studied in this report.

Methods: All the hetero aromatic compounds and N-aniline & N,N-aniline derivatives were optimized at DFT B3LYP/6-31G (2df, p) level of theory using the Gaussian 03 program. The inversion barriers of all the compounds were computed using the G3XMP2 theory.

Results: The amine inversion investigation divulges that the introduction of hetero atom in the ring significantly increases the planarity of the amine group by hyperconjugative effect and resonance effect. Hence pyridine and pyrimidine compounds attain planar configuration. Meanwhile N-methyl aniline and N,N-dimethyl aniline attains planar structure among all the N & N,N-aniline derivatives studied.

Conclusion: Introduction of hetero atom in the ring favours planar amine structure and hence, amino pyrmidines are more planar than the amino pyridine and aniline compounds. Likewise electropositive substituent like methyl group in N-methyl aniline & N,N-dimethyl aniline promotes planar amine structure.

Keywords: Inversion barrier, Amine, Planarity, Aniline, Pyridine, Non-planarity.

INTRODUCTION

The conjugation of an amine group with an aromatic nucleus is one of the most commonly discussed topics in organic chemistry and its attention is usually focused on the chemical reactivity of the aromatic nucleus. On account of the partial conjugation between the amine nitrogen and the aromatic ring, the inversion barrier is very sensitive to changes in the electronic structure of the molecule. So far much less consideration has been given to analyze how the structure and barrier to the inversion of the amine group are changed by the introduction of hetero atom in the ring. The recent past ab initio investigation suggests that the amino groups of nucleic acid bases are inherently nonplanar and flexible [1, 2]. Apparently the nucleic acid bases are the derivatives of aminopyridines and aminopryimidines and hence their investigation on out of plane bending vibration of amine group can further reinforce the non-planar geometry of amino group in the bio-molecules. If it becomes valid, this finding can have important biophysical consequences in the structure of DNA, bio-chemical interactions and molecular recognition process. Analysis of the molecular structure and conformation flexibility of nucleobase analogues has led to the conclusion that non-planar nature of the pyrimidine ring is caused by a deviation of the π character of the cyclic system from the aromatic ring [3, 4].

A microwave study of the 2-aminopyridine has shown that the structure of the amine group in this molecule is non-planar in nature and the same effect could be extended to other amino pyridines as well [5]. Despite its potential significance, the non-planarity of amino group is disregarded due to the lack of reliable spectroscopic data and computational data. The only feasible to way to surmount this limitation can be done by the high level ab initio and DFT calculations. Erstwhile quantum chemical and DFT investigation shows that there is a huge difference in torsion barrier exists between aniline and n-aniline derivatives [6] and therefore its investigation on inversion dynamics has also been extensively studied in this report. This study reports that the methyl group although electron donating group favours planarity in N-methyl aniline and N,N-dimethyl aniline by hyperconjugative effect, this unusual behaviour of methyl group is studied in detail ever first time by G3XMP2 method.

Computational methods

All the pyridine, pyrimidine derivatives and N, & N, N-aniline compounds were optimized at DFT B3LYP/6-31G (2df, p) level of theory using the Gaussian 03 program [7]. The pyridine and pyrimidine substituted prototype molecules were optimized in both planar and non planar structures. No geometrical constraints were imposed to obtain the minimum energy structure of hetero aromatic amines, N-aniline and N, N-aniline derivatives.

The non-planar configuration of aniline molecule is made by placing the nitrogen atom out of plane of benzene ring and for planar structure the amino 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. It is inevitable to include polarizing functions in the calculation of inversion barriers because of the significant changes in hybridization that accompany during nuclear motions. Inversion barrier of various pyridine, pyrimidine derivatives and N-aniline and N,N-aniline derivatives were calculated using the composite G3XMP2 [8] theory and the details of the theory were available in the cited reference.

RESULTS AND DISCUSSION

Inversion barrier of aminopyridines

Introduction of hetero atom nitrogen into the ring has substantial effect on the amine inversion dynamics and structural distortion. The structures of amino pyridines have been shown in figure-1. G3XMP2 investigation of aniline reports that its inversion barrier is 499 cm^{-1} and it agrees well with the experimental value of 523 cm^{-1} [9, 10]. It is clear from table I that the 2-amino pyridine increases the symmetric interaction between carbon and amine nitrogen by decreasing C–N distance from 1.397Å (aniline) to 1.38Å, which conveys that the introduction of nitrogen into the ring increases the delocalization of electron and places the negative charge on the ring nitrogen. The negative charge on the ring produces the resonance effect and consequently reduces the inversion barrier to 296 cm^{-1}.

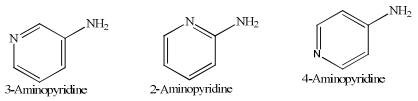

Fig. 1: Structures of amino pyridine

The resonance effect and inductive effect both decreases the electron density around amine nitrogen and as a result it decreases the inversion angle and out of plane angle to 38.3º and 40.38º and causes 2-aminopyridine become more planar than aniline. The 3-aminopyridine has little effect on the inversion dynamics and it yields inversion barrier of 482 cm^{-1}. The replacement of nitrogen at C3 meta position fails to attain planar configuration due to lack of electron delocalization effect and resonance structures. Also it decreases the symmetric interaction between amino group and phenyl ring and thus increases the inversion angle to 41.35**°,** which is higher than the 2-aminopyridine of 38.3**°.** It apparently insights that the 3-aminopyridine has little influence on the amine structure due to nitrogen at meta position and hence, its inversion barrier is as same as aniline molecule. The 4-aminopyridine favors the planar structure by decreasing the inversion barrier from 499 $cm^{-1}$to 243 cm^{-1}. The presence of electronegative nitrogen at the para position decreases the electron density by placing the negative change on the ring nitrogen and produces the resonance effect and inductive effects through σ bond and yields low inversion barrier [11] of 243 cm^{-1}. The presence of nitrogen atom at the para position increases the symmetric interaction between carbon and amine nitrogen by decreasing the C–N bond distance from 1.397Å to 1.38Å. This interaction facilitates the π-effect and decreases the inversion angle and out of plane angle and promotes planar amine structure. Among all the aminopyridines 4-amino pyridine scores low inversion barrier due to strong π-π interaction and resonance effect; hence it becomes more planar than aniline and other pyridines. The inversion and geometrical parameter of amino pyridines agrees well with spectral studies [12].

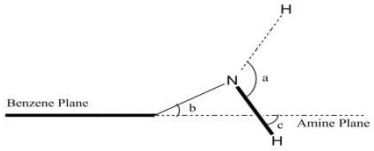

Fig. 1: Structure of amine group

The structure of amine group is shown in the fig. 1 and it delineates that the nitrogen atom of the amino group is tilted away 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 key structural parameter used to measure the pyramidalization of the amine group.

Inversion barrier of aminopyrimidines

The amino pyrimidines are the important nucleic acid bases and its degree of non-planarity is intrigue in nature and hence, it is analyzed by the ab initio and DFT method by using composite G3XMP2 method. The recent quantum chemical investigation on aminopyrimidines reveals that pyrimidine ring possess remarkable degree of conformational flexibility, despite its aromatic character with two nitrogen atom in the ring, furthermore it indicates that pyrimidines are more planar than pyridine and aniline molecules [13]. The structures of amino pyrimidines have been shown in figure-2.

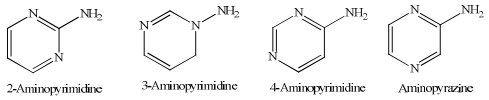

Fig. 2: Structures of Aminopyrimidine

Fig. 2: Structures of Aminophyrimidine

Aminopyrimidines have substantial effect on the inversion barrier and geometry of the amine structure due to the presence of two nitrogen atoms in the ring. The 2-aminopyrimidine underscores low inversion barrier of 68.85 cm^{-1} among all the hetero aromatic amines. The presence of two nitrogen atoms in the phenyl ring strongly promotes the electron delocalization by resonance effect and negative inductive effect, these two effects disperses the electron density around amine nitrogen and promotes the planar amine structure. This causes the transformation of single bond (C–N) to partial double bond character of (1.397Å to 1.36Å), and accounts for low inversion barrier and perfect planar configuration of amine group. The two nitrogen atoms in the phenyl ring decreases the tilt angle from 2.5° to 1.26° due to the π-effect and releases the NHN bond angle strain and imparts additional planarity. Furthermore it is apparent from table I that the 2-amino pyrimidine decreases the out of plane angle from 44.85° to 28.54° due to the opening HNH bond angle, thereby it makes the amine group more planar than amino pyridine and aniline molecule. The 4-aminopyrimidine molecule also acquires low inversion barrier of 89.62 cm^{-1} and attains more planar configuration than aniline and hetero aromatic amines. Amino pyrimidines generally have low out of plane angle and low inversion barrier due to the replacement of hydrogen atom by nitrogen atoms in the ring; this two nitrogen atom disperses the electron density around amine nitrogen by negative inductive and resonance effects. The only exception is 3-aminopyrimidine because it yields high inversion barrier of 433 cm^{-1}. It is due to the position of nitrogen atoms in the ring and thus it fails to produce resonance structures; as a result it undermines the electron delocalization process and becomes non-planar. However, 3-aminopyrimidine attains same planar configuration with aniline molecule due to the presence two nitrogen atoms in the ring.

Table 1: Geometrical parameters of amino-pyridines & pyrimidines

Molecule	d(C–N) Å	H-N-H Angle°	Inversion angleº (a)	Tilt angle° (c)	Out of plane angleº (b)	Inversion barrier (cm^{-1})
Aniline	1.397	111.17	42.35	2.5	44.85	499
2-Aminopyridine	1.38	114.34	38.30	2.08	40.38	296.11
3-Aminopyridine	1.39	111.46	41.35	2.485	43.835	481.78
4-Aminopyridine	1.38	113.24	35.87	2.14	38.01	243.21
2Aminopryimidine	1.36	118.44	27.28	1.26	28.54	68.85
3aminopyrimidine	1.388	111.85	39.90	2.34	42.23	432.87
4Aminoprymidine	1.36	116.72	28.73	1.68	30.41	89.62
Aminopyrazine	1.370	114.92	35.55	2.06	37.61	230.50

Table 1, clearly shows that the aminopyrazine involves in asymmetric interaction between amine group and phenyl ring by increasing C–N bond length from 1.26Å to 2.06Å in relative to other amino pyrimidine and thus increases the inversion barrier from 89.6 $cm^{-1}$to 231 cm^{-1}. Despite, it attains more planar configuration relative to the parent aniline molecule by resonance effect and negative inductive effect. Invariably all the amino pyrimidine increases the planarity due to the presence of two nitrogen atom in the ring and promotes symmetric interaction between amine nitrogen and phenyl ring by the conformational flexibility.

Inversion studies of N-aniline & N,N-aniline derivatives

The partial replacement of hydrogen atom by methyl group in aniline molecule has huge impact on inversion dynamics and geometry of the structure, consequently it leads to the planar amine configuration [14] and its structure is shown in fig.-3. The N-methyl

group disperses the electron density around the amine nitrogen by steric and hyper conjugative effect and reduces inversion barrier to 187 cm^{-1}, which ultimately imparts planar amine configuration. The presence of methyl group decreases electron density around amine nitrogen and increases the NHN bond angle by releasing angle strain from 111.2º to 114.7º. The increase in NHN bond angle decreases the out of plane angle from 44.85º to 33.43º and places the n-methyl amine in ring plane by promoting planar amine structure. In summary, the investigation found that the n-methyl aniline enhances the planar configuration by hyperconjugation effect [15]. Furthermore, table II authenticates that the wide opening of HNH bond angle decrease the out of plane angle, tilt angle and inversion angle, thereby it accounts for additional planarity than the parent aniline molecule. N,N-dimethyl aniline further lowers the inversion barrier to 64 $cm^{-1}$and it is the lowest among all the N & N,N-aniline derivatives.

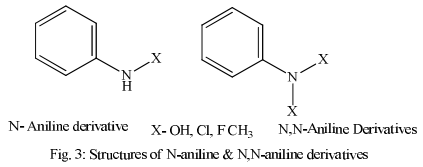

Fig. 3: Structures of N-aniline & N,N-aniline derivatives

Fig. 3: Structure of N-aniline and N, N aniline derivatives

It appears that two methyl groups attached to the nitrogen atom experience strong steric hindrance and hyperconjugative effect; these two effects causes wide opening of NHN bond angle from 111.2º to 118º and concurrently reduces the tilt angle, inversion and out of plane angle, this structural alteration makes the di-methyl amine to attain full planar amine structure.

This unusual phenomenon of methyl group is attributed to the mutual transfer of π charges of the methyl group and σ charges of the aromatic system [16]; so there is no room to increase electron density around nitrogen atom of the amino group and subsequently offers perfect flat amine structure. Substitution of fluorine atom by an amine hydrogen atom steeply increases the torsion barrier from 499 $cm^{-1}$to 3,382 cm^{-1}.

Replacement of fluorine atom increases the asymmetric interaction between amine nitrogen and phenyl ring; thereby it increases the bond C–N bond length from 1.397Å to 1.41Å. This interaction promotes sp^3 hybridization and accounts for closure of NHN bond angle from 111° to 102° and thus heavily deviates from the ring plane by attaining highly non-planar configuration. So in summary N-fluoroaniline drastically increases the inversion barrier and attains pyramidal configuration due to strong steric repulsion. It is well established that N-fluorination of aniline destabilizes the structure; whereas ring fluorination enhances the stability [17] and this investigation authenticates it.

Table 2: Geometrical parameters of N & N,N-aniline derivatives

Molecule	d(C–N) Å	HNH Bond Angleº	Inversion angle°(a)	Tilt angleº(c)	Out of plane angleº (b)	Inversion Barrier (cm^{-1})
Aniline	1.397	111.17	42.35	2.5	44.85	499
N,N-difluoroaniline	1.448	102.53	63.18	6.17	69.35	10,688
N-fluoroaniline	1.410	102.800	57.502	4.67	62.172	3,382
N,N-dimethylaniline	1.380	118.473	15.624	0.36	15.98	64.46
N-methylaniline	1.388	114.700	31.39	2.04	33.43	187
N,N-dichloroaniline	1.441	107.02	48.63	7.385	56.015	2,674
N-hydroxyaniline	1.410	105.91	52.32	3.83	56.15	2,136

The N,N-di-fluoroaniline further increases the torsion barrier three fold of N-fluoroaniline to 10,688 cm^{-1}due to the heavy steric repulsion between two fluorine atoms. The fluorine atoms attached to the amine nitrogen makes it electron rich centre and as a result it decreases the C–N interaction and deviates from the phenyl ring plane; therefore it attains highly pyramidal configuration. The massive torsional barrier difference between N-fluoroanile and N,N-difluoroaniline leads to the formation of isomers and hence both the compounds can acts as a isomeric compounds. Besides, table II depicts that the N,N-difluoroaniline increases the HNH torsion angle from 42º to 63º and tilt angle from 2.5° to 6°, this huge deviation places amine nitrogen away from the plane and destabilizes the compound. It is clear from table II that the N,N-difluoro aniline lengthens the (C–N) bond length from 1.38Å to 1.45Å and so transforms the partial double bond character of (C–N) to single bond.

This results in poor delocalization of electron between the amine group and phenyl ring; which makes the compound non-planar and rigid. Substitution of hydroxyl group by amine hydrogen atom enormously increases the inversion barrier from 499 $cm^{-1}$to 2,136 cm^{-1}. This steep rise in inversion barrier is mainly due to donation of π-charges from oxygen to amine nitrogen. The heavy electron density around amine nitrogen causes steric repulsion and hinders the tunnelling of electrons; so this cummulative effect causes highly non-planar configuration of the amine structure. The recent ab initio & DFT investigation of amine inversion reveals that the electron withdrawing substituents in the ring promotes the planarity and stabilizes the molecule [18].

However, it is quite strange to note that the electron negative substituents in N,N-aniline derivatives increases the inversion barrier and favors the completely non-planar configuration; whereas electron donating substituents replacing the amine hydrogen atom decreases the inversion barrier and accounts for planar amine configuration. The electronegative substituent in the ring decreases the torsion barrier by inductive effect and resonance effect; whereas it increases the torsion barrier when it is replaced by amine hydrogen by steric effect. The investigation further unearth that the electro negative substituents replaced by amine hydrogen largely increases the inversion barrier and leads to the forlmation of isomeric compounds such as pyramidal and planar forms.

CONCLUSION

Ab initio and DFT investigation of hetero aromatic amines concludes that the 2-aminipyridine and 4-aminopyridine favors planar configuration by decreasing the inversion barrier by the inductive effect and resonance effect imparted by nitrogen atom in the ring. However in case of pyrimidine compounds 4-aminopyrimidine and aminopyrazine compound attains full planar configuration due to the strong π-π interaction and negative inductive effect produced by nitrogen atom in the ring. The investigation further concludes that the presence of nitrogen in the aromatic ring decreases amine torsion barrier and promotes planar amine structure by resonance effect. Hence hetero aromatic amines are more planar than aniline and other aromatic amines. Meanwhile, the investigation of inversion dynamics in N–aniline and N,N-aniline derivatives reveals that the replacement of amine hydrogen atom by electronegative substituents enormously increases the inversion barrier by steric effect and repulsive effect and attains complete non-planar configuration. It further discloses that the planar and pyramidal configuration of electronegative substituents acts two separate isomeric compounds in N-aniline & N,N-aniline derivatives. However, the electron donating substituents decreases the barrier by strong hyperconjugative effect & π-charge effects and attains

planar amine configuration. The investigation finally concludes that the substituent replacing the amine hydrogen have profound effect on inversion dynamics, especially electron donating substituents imparts full planar amine configuration. The results of G3XMP2 inversion dynamics of amine studied in this report will have greater impact on DNA base pairing, configuration of nucleobases, molecular recognition process and hydrogen bonding interactions.

CONFLICT OF INTERESTS

Declared None

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