

封面：

分类号_____

密级_____

U D C_____

编号_____

厦 门 大 学

博 士 后 研 究 工 作 报 告

**Main Group Organic Isomers: Probing the Origin of
Thermodynamic Stabilities, and Finding Influence of Aromaticity**

博 士 后 姓 名： Muhammad Rouf Alvi

流动站（一级学科）名称： 化学系

专 业（二级学科）名称： 有机化学

研究工作起始时间 2016 年 01 月

研究工作期满时间 2017 年 12 月

厦 门 大 学

2018 年 01 月

厦门大学博士后研究工作报告

著作权使用声明

本人完全了解厦门大学有关保留、使用博士后研究工作报告的规定。厦门大学有权保留并向国家主管部门或其指定机构送交该报告的纸质版和电子版,有权将该报告用于非赢利目的的少量复制并允许该报告进入学校图书馆被查阅,有权将该报告的内容编入有关数据库进行检索,有权将博士后研究工作报告的标题和摘要汇编出版。保密的博士后研究工作报告在解密后适用本规定。

本研究报告属于: 1、保密 (), 2、不保密 ()

纸本在 年解密后适用本授权书;

电子版在 年解密后适用本授权书。

(请在以上相应括号内打“√”)

作者签名: 日期: 年 月 日

导师签名: 日期: 年 月 日

Abstract

Current postdoctoral research report is comprised of theoretical demonstration of thermodynamic stabilities of the main group organic compounds, evaluation of aromaticity, and prediction/explanation of organic reaction pathways with prospect of targeted outcomes. A brief introduction to the work performed is given below.

The BN-doped organic analogues are interesting as aliphatic amineboranes for hydrogen storage, precursors for aromatic borazines and adsorbent cage azaboranes. However, BN-doped aliphatic polyenes remained undeveloped. In this study, we perform theoretical calculations on two mono BN-doped aliphatic lower polyenes, 1,3-butadiene and 1,3,5-hexatriene. A general rule is proposed in order to predict the relative thermodynamic stabilities of their isomers. Rules established here may lead researchers to synthesize isomers of BN-doped polyenes with particular thermodynamic stability.

Azirines, nitrogen containing heterocyclic analogues of cyclopropenes, generally find their use as reactive intermediates in synthetic organic chemistry. They exist in two tautomeric forms: *1H*-azirine (0.0 kcal/mol) is generated *in situ* and readily rearranges to more stable (and sometimes isolable) *2H*-azirine (-34.7 kcal/mol). Therefore, our current DFT investigations are focused on developing a strategy to stabilize *1H*-azirine, and hamper its tautomerization to *2H*-azirine. This study highlights the proper combination of both electronic and steric factors that along with aromaticity play significant role in stabilizing *1H*-azirines. Our findings are intriguing for researchers to realize first isolable *1H*-azirine experimentally.

Pyrrole, one of the important class of heterocyclic compounds, exists in three tautomeric forms; *1H*-pyrrole most stable tautomer due to its higher aromatic character as compared to the other two, *2H*- and *3H*-pyrroles (both antiaromatic). The availability of relevant synthetic data also depicts their thermodynamic stabilities. Although few theoretical studies are available, however, no significant effort has been directed to tune and explain the origin of the relative stabilities of these tautomers. Therefore, in our current theoretical investigation, we determined aromaticity is the major stability controlling force. However, an electron withdrawing substituent can reverse the above-mentioned stability order, i.e., forcing *1H*-pyrrole to the least stable position (even though the most aromatic). In the latter case, bond dissociation energy (BDE) instead of aromaticity controls the stability order.

Keywords: DFT, thermodynamic stability, polyene, pyrrole, azirine.

厦门大学博硕士学位论文摘要库

目 录

目 次

1 Introduction.....	3
2 Computational Details.....	6
3 Probing a General Rule towards Thermodynamic Stabilities of Mono BN-doped Lower Polyenes.....	7
3.1 Introduction.....	7
3.2 Results and Discussion.....	7
3.2.1 BN-doped Butadiene (BH).....	7
3.2.2 BN-doped Hexatriene (HH).....	9
3.3 Conclusion.....	10
4 Hampering Tautomerization of 1 <i>H</i> -azirine to 2 <i>H</i> -azirine.....	11
4.1 Introduction.....	11
4.2 Results and Discussion.....	11
4.2.1 Screening of Migrants.....	11
4.2.2 Screening of Substituents.....	12
4.2.3 Combined Electronic and Steric Effect on Boryl Migrant...12	
4.3 Conclusion.....	13
5 Theoretical Study to Discern the Origin of Relative Thermodynamic Stabilities of Pyrrole Tautomers.....	14
5.1 Introduction.....	14
5.2 Results and Discussion.....	15
5.2.1 Relative Thermodynamic Stabilities.....	15
5.2.2 Activation Barriers.....	16
5.3 Conclusion.....	16
参考文献(References).....	17
致谢(Acknowledgements).....	21
博士生期间发表的学术论文、专著.....	22
博士后期间发表的学术论文、专著.....	23
个人简历(CV).....	24
联系地址 (Contact Address).....	25

说 明

博士后研究工作报告的排版以全国博士后管理委员会办公室制定的统一格式为准（参见以上排版范例），研究报告封面统一以彩色羊皮卡纸制作，颜色不限，内页用纸为普通 A4 打印纸，单面或双面打印不限，正文字体为宋体小四。

为更好地保护博士后研究报告的著作权，请各位博士后在博士后研究工作报告中文摘要前加做《厦门大学博士后研究报告著作权使用声明》（具体格式见附件 2），并在该声明中明确保密年限。

出站时，提交 1 份研究报告至厦门大学图书馆，2 份给厦门大学人事处博士后管理办公室（学校定期提交给国家图书馆）。

厦门大学博硕士论文摘要库

1. Introduction

In silico study of chemistry (i.e., computational chemistry) involves the study of structure, bonding, properties, and reactions of compounds *via* quantum chemical methods. Nowadays, availability of high-speed computers and refined computational tools have made computational chemistry an essential part of almost every scientific report to (solely or augmented with experiments) explain physical and chemical properties of materials. In organic chemistry, computational methods excellently deal with the study of organic reactions, mechanisms, and targeted synthesis *via* probing stability, physical properties and chemical reactivities of organic compounds. Since current report comprised of theoretical demonstration of thermodynamic stabilities of isomers of the main group organic compounds, such as, BN-doped lower polyenes, azirines and pyrroles. Therefore, the origin of relative thermodynamic stabilities of the above isomers is explained based on the concepts (where applicable) of structure, bonding, electronegativities, atomic charges, resonance, and aromaticity. Quantum chemical methods applied in this report are described within chapter 2.

Aminoborane ($\text{H}_2\text{N}-\text{BH}_2$), isoelectronic to ethylene ($\text{H}_2\text{C}=\text{CH}_2$), were first detected as transient species in 1952 (**A**) [1] and were later isolated (**B**, **C** and **D**) (Fig. 1.1) [2]. Meanwhile, it was elucidated that B-N bond was locked to free rotation *via* coordinate covalent bond formed by the donation of nitrogen lone pair to electron deficient boron [2b,3]. Aminoboranes are highly sensitive to moisture and air, readily dimerize and cyclize depending on steric bulk. Therefore, these species are mainly interesting for transition metal-catalyzed reactions [4], source for linear diborazanes ($\text{R}_3\text{N}-\text{BH}_2-\text{NR}_2-\text{BH}_3$) or oligoborazanes [5], cyclic adducts like cyclic (cage) azaboranes [6], and borazines (B-N homologue of benzene) [7,8]. Recently, boron-incorporated compounds received significant attention in biomedical research [9] and optoelectronic materials [10]. Amineboranes ($\text{H}_3\text{N}-\text{BH}_3$), and aminoboranes ($\text{H}_2\text{N}-\text{BH}_2$) have been targets for hydrogen storage [11]. Since the first example of BN-doped butadiene (vinylaminoborane **E**, Fig. 1.1) was reported in 1964 [12], the follow-up studies are very limited [13]. However, fundamental issue of the relative thermodynamic stabilities of various isomers for mono BN-doped lower polyenes remained unclear. Therefore, to address this issue, we perform density functional theory (DFT) calculations on mono BN-doped 1,3-butadiene and 1,3,5-hexatriene. Consequently, we propose a general rule to predict the relative thermodynamic stabilities of these isomers (details in chapter 2).

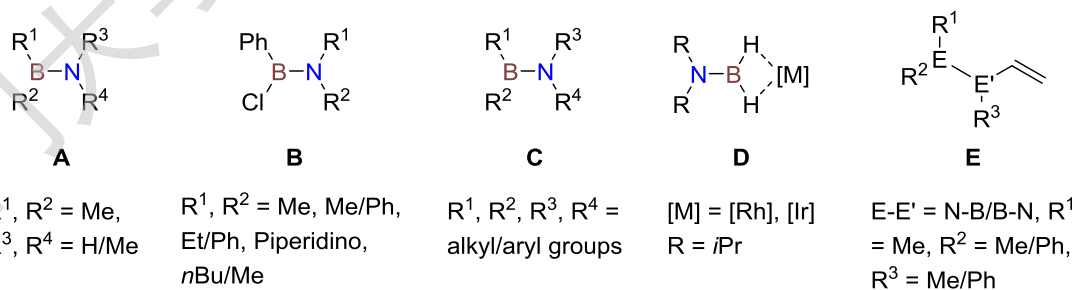
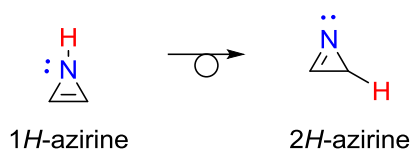


Fig. 1.1. Alkylaminoboranes **A** – **D** (isoelectronic to ethylene), and vinylaminoborane **E** (isoelectronic to butadiene).

Azirine, heterocyclic analogues of three-membered ring cyclopropene, exists in two tautomeric forms; *1H*-azirine, comprised of an amine group and a carbon-carbon double bond, which readily rearranges to more stable (and sometimes isolable) *2H*-azirine, with an imine group and a saturated carbon (Scheme 1.1).



Scheme 1.1: Tautomerization of *1H*-azirine to *2H*-azirine.

2H-azirine is not only generated as reactive intermediate but also available through a variety of sources [14]. To best of our knowledge, no *1H*-azirine has been isolated yet, since it readily tautomerizes to more stable *2H*-azirine [15]. Although, few claims existed [16] which were latter rejected on solid technical grounds [17]. The instability of *1H*-azirines is attributed to the antiaromatic character of the planar ring system with 4π electrons. Earlier, molecular orbital calculations confirmed destabilizing interaction between the π -bond electrons and lone-pair of nitrogen [18]. These calculations predicted a non-planar structure for *1H*-azirine, with an unusually high barrier (35.2 kcal/mol) to inversion about nitrogen. Therefore, it is challenging to stabilize *1H*-azirine and hamper its tautomerization to *2H*-azirine. However, it is anticipated that any group that can reduce electron density on *1H*-azirine's nitrogen can minimize antiaromatic interaction between lone pair of nitrogen and the ring π -electrons, as a result, it can increase stability of *1H*-azirine as compared to its tautomer *2H*-azirine. The very few examples of short-lived *1H*-azirines detected at very low temperatures by IR and UV spectroscopy, indicating electron-withdrawing cyano group could be the reason behind their stability by reducing their antiaromatic character [19]. Since no solid efforts have been made in favor of *1H*-azirine stabilization in order to keep its tautomerization at check. Therefore, we performed theoretical investigations to address this urgent issue. In this regard, we systematically utilized groups of varied electronic nature, not only as migrants (from N to C), but also as substituents on carbon(s) of azirines to realize their ability to resist or facilitate tautomerization of *1H*-azirine to *2H*-azirine (details in chapter 3).

Pyrrole exist in three tautomeric forms (Fig. 1.2a); *1H*-pyrrole (with 6π -electrons, aromatic), *2H*- and *3H*-pyrrole, also called isopyrroles or pyrrolenines (4π -electrons and a saturated carbon, antiaromatic). Earlier theoretical study conducted by Schuster et al. in 1979 to find energetic relationships between pyrrole tautomers at simple theoretical method MINDO/3 (limit of that time) [20]. They evaluated the relative thermodynamic stabilities of *1H*- and *2H*-pyrrole for H, and Me shifts, and found that the former was more stable than the latter (Fig. 1.2b). The stability of *1H*-pyrrole is intuitively attributed to its aromatic character [21] that is lacking in the other two tautomeric forms; *2H*- and *3H*-pyrrole.

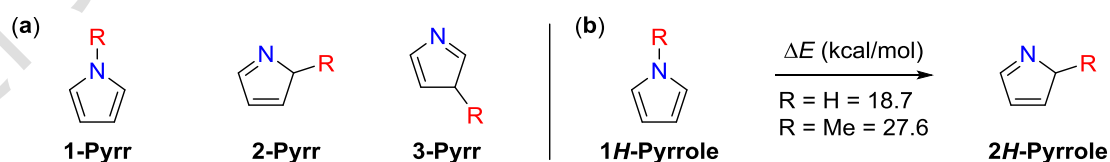


Figure 1.2: (a) Pyrrole tautomers. (b) Thermodynamic stabilities of *1H*- and *2H*-pyrroles by Schuster et al.

Later, in 1987 and 1990, Chiu and Sammes experimentally described that *2H*- and *3H*-pyrroles could exist in equilibrium and each tautomer could rearrange further to more stable *1H*-pyrrole [22]. A subsequent theoretical study at HF/6-31G(d) and MP2/6-31G(d) by Bachrach in 1993 not only

supported previous findings, mentioned above, but also evaluated energetic details of sigmatropic hydrogen shifts in pyrroles [23]. The synthetic ease of pyrrole tautomers is found related to their relative thermodynamic stabilities. That is why, significant experimental data is available for the most stable isomer *1H*-pyrrole followed by the second most stable isomer *2H*-pyrrole [24]. However, availability of *3H*-pyrrole is existed through steric means [25] due to its readily conversion to the more stable *2H*-pyrrole through low activation barrier [26]. Although tautomerization energies (i.e., relative thermodynamic stabilities) and relevant activation barriers of pyrrole isomers has been studied earlier at certain occasions of time, discussed above. However, no effort has been depicted to explain the origin of relative thermodynamic stabilities of these tautomers. Therefore, currents theoretical investigation is not only focused on explaining the origin of the relative thermodynamic stabilities of pyrrole tautomers but also tuning those stabilities to make the least stable isomer the most stable one (details in chapter 4).

廈門大學博碩士論文摘要庫

2. Computational Details

All structures are optimized in the gas phase by Minnesota hybrid meta density functional theory method of Zhao and Truhlar M06-2X [27], using the 6-311G(d,p) basis set [28] with an ultrafine grid. Frequency calculations are performed at the same level of theory to identify all stationary points as minima (zero imaginary frequency and one imaginary frequency for transition state).

Single-point energy calculations are performed at the CCSD(T)/6-311G(d,p) level [29] for all structures of BN-doped lower polyenes, relative energies and natural charges are reported on this method throughout this study. The natural resonance theory (NRT) [30] analysis within the NBO 6.0 program [31] is used to estimate resonance weights of individual resonance structures.

However, thermodynamic stability comparison for the azirine and pyrrole isomers is achieved at DFT level. Reliability of DFT results is confirmed at single-point CCSD(T) level with the same basis set for comparing selective isomers from each class of compounds. For instance, azirine **1-H** is more stable by 34.7 kcal/mol than **2-H** (Fig. 4.1) at M06-2X that is consolidated when CCSD(T) also gives very close agreement (36.5 kcal/mol). Similarly, relative energies of **1-Pyrr-H**, **2-Pyrr-H** and **3-Pyrr-H** (Fig. 5.2) at M06-2X (0.0, 17.3 and 18.7 kcal/mol, respectively) find good correlation with the single-point CCSD(T) energies (0.0, 11.6 and 13.4 kcal/mol, respectively).

All calculations are performed with Gaussian 09 program [32], except Mayer's bond orders that are computed by the Multiwfn package [33]. Furthermore, transition states (TSs) confirmations are performed through intrinsic reaction coordinate (IRC) [34] with G03 program [35] at B3LYP method [36], and the intermediates resulted from IRC calculations are subsequently optimized at M06-2X with G09 program to keep all computational data consistent at M06-2X level. In order to estimate aromaticity of the azirines and pyrrole isomers, we calculated nucleus-independent chemical shifts (NICS) using the gauge including atomic orbitals (GIAO) method [37] at 6-311G(d,p) basis set. The NICS(1)_{zz} is preferred owing to being one of the best NICS methods employed to estimate aromaticity [38].

3. Probing a General Rule towards Thermodynamic Stabilities of Mono BN-doped Lower Polyenes

Quantum chemical calculations have been carried out at CCSD(T)/6-311G(d,p)//M06-2X/6-311G(d,p) on two aliphatic mono BN-doped lower polyene (1,3-butadiene and 1,3,5-hexatriene) isomers in order to predict a general rule towards their relative thermodynamic stabilities.

3.1 Introduction

The isoelectronic nature of B–N bond to that of C=C bond led to the BN-doped organic analogues with orthogonal properties, which attracted prominent interest of researchers for decades. For example, aliphatic amineboranes are interesting for hydrogen storage [11] and the precursors for aromatic borazines [7,8] and adsorbent cage azaboranes [6]. However, BN-doped aliphatic polyenes remained undeveloped. In current density functional theory (DFT) study, BN-doped isomers of two lower polyenes (1,3-butadiene and 1,3,5-hexatriene) are investigated in order to propose a general rule to predict their relative thermodynamic stabilities.

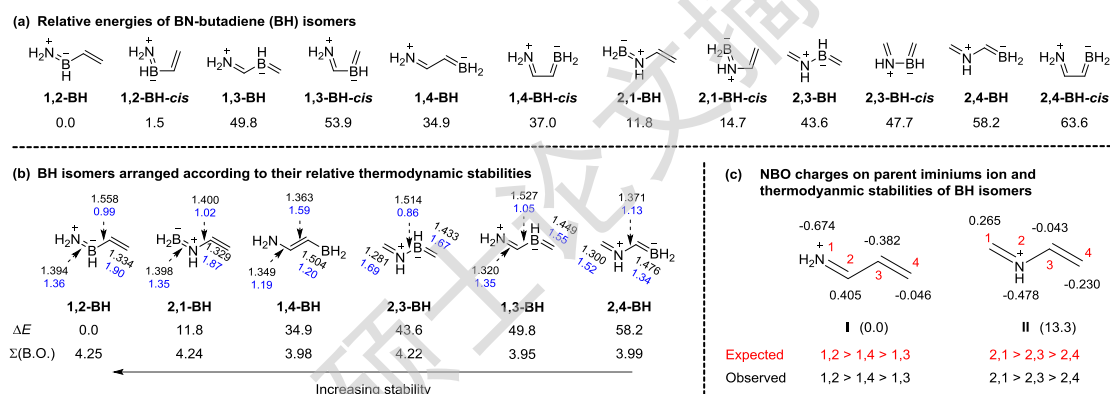


Fig. 3.1: (a) Relative energies of *cis*- vs *trans*-isomers. (b) BH isomers arranged according to relative thermodynamic stability. Bond lengths (Å) and Mayer's bond indices are given in black (above) and blue (below), respectively. $\Sigma(\text{B.O.})$ is the sum of all central Mayer's bond indices. NBO charges are provided for all atoms except hydrogens. (c) NBO charges in N-doped butadiene isomers, i.e., parent iminium ion. Expected (red) and observed (black) relative stability trends of BN-doped isomers based on NBO charges are given. The two numbers in each trend show relative position of N and B, respectively, in a particular isomer. Relative energies of isomers **I**, and **II** are also given (in parenthesis).

3.2 Results and Discussion

3.2.1 BN-doped Butadiene (BH)

Since *s-trans* isomers are energetically more stable than *s-cis* isomers (Fig. 3.1a), we only considered the former cases for our entire investigations.

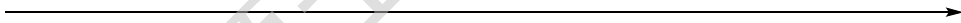
Computational results indicate that isomers with terminal nitrogen are more stable than their inverse analogues (where boron is at the terminal position) (Fig. 3.1b). Consequently, **1,2-BH** and **1,3-BH** possess higher thermodynamic stabilities by 11.8 and 8.4 kcal/mol, respectively, as compared to their inverse isomers **2,1-BH** and **2,4-BH**. Isomers with B and N directly connected are more stable than the disconnected ones [4]. This argument is supported by the observation that the B and N directly connected isomers (**1,2-BH**, **2,1-BH**, and **2,3-BH**) have higher thermodynamic stability than the B and

N disjointed isomers (**1,3-BH** and **2,4-BH**). Surprisingly, anomalous behavior is observed for **1,4-BH**, an isomer with both B and N at terminal positions that is more stable by 8.7 kcal/mol than **2,3-BH**, an isomer with a central B-N connection. This anomaly can be attributed to the better delocalization of π -electrons in **1,4-BH** which held intermediate bond character between single and double bond (Fig. 3.1b). Note that the total bond order of **1,4-BH** (3.98) is less than that of **2,3-BH** (4.22). Therefore, bond dissociation energies (BDEs) have been considered to gain an insight into the stabilities of these species (discussed *vide infra*).

NBO charges calculated for BN-doped structures do not provide reasonable correlation with the thermodynamic stabilities of the corresponding isomers within a polyene (Fig. 3.1b). However, the NBO charges observed on the parent iminium ion carbons (i.e., N-doped butadiene, prior to B-doping) can precisely predict the incoming boron at a particular position, thus leading to isomers of expected (relative) thermodynamic stability (Fig. 3.1c).

To probe the origin of significant difference (11.8 kcal/mol) on thermodynamic stability between **1,2-BH** and **2,1-BH**, we replace vinyl (sp^2 hybridized) group with various substituents. Specifically, we utilized two simple isomers, $H_2N-BH-R$ and $H_2B-NH-R$, respectively, where R = F, OH, Cl, NH_2 , Br (electronegative), SiH_3 and, BH_2 (electropositive) groups (Fig. 3.2).

	R	F	OH	Cl	NH_2	Br	CH_3	$HC=CH_2$	H_2C-CH_3	SiH_3	BH_2
	E.N.	4.00	3.51	3.00	2.61	2.80	2.27	2.31	2.28	2.21	2.09
$H_2N=BH-R$	ΔE	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
$H_2B=NH-R$	ΔE	100.1	83.2	67.9	59.7	59.4	16.0	11.8	11.4	-11.3	-31.7



 Increasing stability of $H_2B-NH-R$ relative to $H_2N-BH-R$ isomer

Fig. 3.2: Substituent effect on the relative thermodynamic stability of $H_2N-BH-R$ compared to its inverse isomer $H_2B-NH-R$ analyzed by electronegativities (E.N.). The relative energies are given by kcal/mol.

Increased ionic (or reduced covalent) character of B/N-R bond tunes the relative thermodynamic stabilities of the two isomers $H_2N-BH-R$ and $H_2B-NH-R$. Fig. 3.2 describes electronegativities (E.N.) with respect to the scales developed by Huheey for individual atoms and groups [39]. More electronegative group at B increases ionic character of B-R bond, leading to higher thermodynamic stability of $H_2N-BH-R$ isomer. Consequently, an enhanced destabilization is observed for its inverse isomer $H_2B-NH-R$ where the N-R bond becomes more covalent due to the reduced E.N. difference between N and R group. On the other hand, highly electropositive group at N in $H_2B-NH-R$ isomer increases its stability. For instance, F enhances thermodynamic stability of $H_2N-BH-R$ isomer by approximately by 100 kcal/mol than its inverse isomer $H_2B-NH-R$. On the other hand, a considerable reduction in the thermodynamic stability (11.3 kcal/mol) of $H_2N-BH-R$ is observed when the SiH_3 group replaces F.

In a word, we can conclude that a substituent R with higher E.N. than boron stabilizes $H_2N-B(H)-R$ isomer over its inverse $H_2B-N(H)-R$, thus supporting the stability of **1,2-BH** over **2,1-BH**. Additionally, collective bond dissociation energies (BDEs) of three central bonds (467.7 and 433.0 kcal/mol, respectively) also support stability of **1,2-BH** over **2,1-BH**. Similarly, collective bond dissociation energies (BDEs) of three central bonds (423.0 vs 366.3, and 373.4 vs 350.6 kcal/mol,

respectively) for **1,4-BH** vs **2,3-BH**, and **1,3-BH** vs **2,3-BH** support their relative thermodynamic stabilities.

3.2.2 BN-doped Hexatriene (HH)

Fifteen isomers are possible by BN-doping in 1,3,5-hexatriene (Fig. 3.3a). Relative stability of pairs of isomers with inverse B and N positions is such that isomer with N at the terminal position is always by 8.3 – 13 kcal/mol more stable than the isomer with B at the terminal position. Such as **1,2-HH** and **2,1-HH**, **1,4-HH** and **3,1-HH**, **1,5-HH** and **2,6-HH**, and this agrees with relative stability of parent iminium ions, shown in Fig. 3.3b. As mentioned, **2,3-HH** and **3,2-HH** are of comparable stability, and the same is the case for **2,4-HH** and **3,5-HH**. The least stable isomer possesses terminal methylene at both B and N, **2,5-HH**. Similarities are observed between BN-butadiene and BN-hexatriene isomers with respect to their structure and relative thermodynamic stabilities. For instance, isomer **1,2-HH** with terminal N-B connection is the most stable among all BN-hexatriene isomers (Fig. 3.3c) that is similar to **1,2-BH** with the same terminal N–BR connection being the most stable among all BN-butadiene isomers (Fig. 3.3c). Additionally, **1,2-HH** isomer is 13.0 kcal/mol more stable than its inverse **2,1-HH** (with B–NR connection). This energy difference is also close to that (11.8 kcal/mol) found between **1,2-BH** and its inverse isomer **2,1-BH**. The NBO charges observed on the parent iminium ion carbons (i.e., N-doped hexatriene, prior to B-doping), as observed above for BH-isomers, can precisely predict incoming boron(s) at particular position(s), thus leading to isomer(s) of expected (relative) thermodynamic stability in BN-doped hexatriene (Figs. 3.3b, and 3.3c).

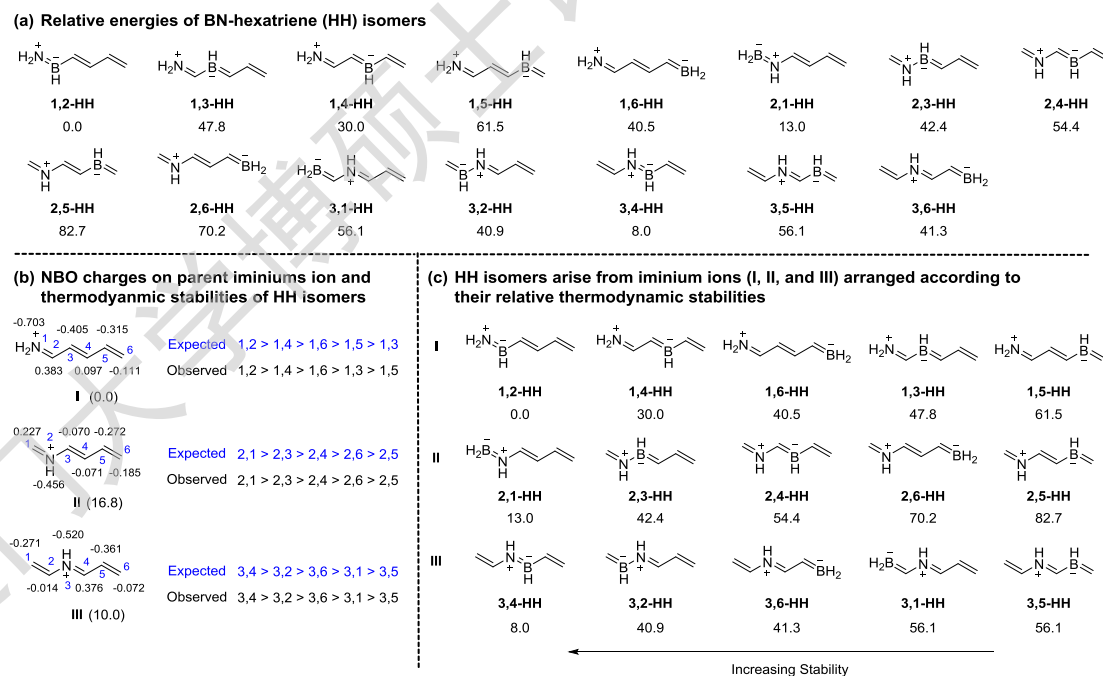


Fig. 3.3: (a) relative energies of all fifteen HH-isomers. (b) NBO charges in N-doped hexatriene isomers. Relative energies are provided in parenthesis. Expected (blue) and observed (black) relative stability trends (of BN-doped isomers on the basis of NBO charges) are given. (c) BN-doped hexatriene isomers generated from N-doped structures (**I**, **II**, and **III**) are arranged by their decreasing order of relative stability.

Only one anomaly is observed where relative thermodynamic stabilities of isomers **1,3-HH** and **1,5-HH** are opposite to that predicted based on NBO charges on iminium ion **I** (Fig. 3.3). More

delocalization in **1,3-HH** could be one of the reasons for its higher thermodynamic stabilization compared to **1,5-HH** that is supported by bond orders and natural atomic orbital occupancies [$2p\pi$] NAOOs (Figure 3.4). NBO charges also support less charge separation in **1,3-HH** (from -0.745 to +0.145) than **1,5-HH** (from -0.788 to +0.279).

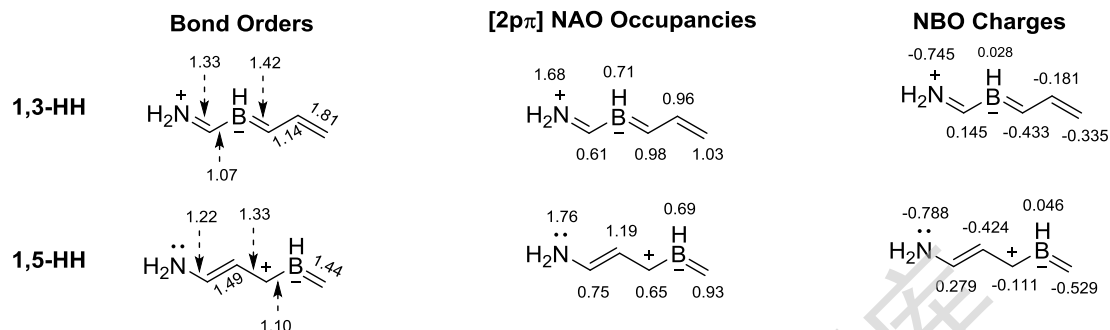


Fig. 3.4: Bond Orders, [$2p\pi$] NAO occupancies (e) and NBO charges for **1,3-HH** and **1,5-HH** are given for all atoms except hydrogens.

3.3 Conclusion

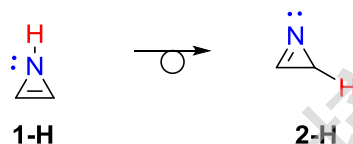
In conclusion, a general rule is proposed that can predict relative thermodynamic stabilities of two lower polyene isomers based on structural similarities. For example, isomers with terminal N (directly BN-connected) are of significant thermodynamic stability than their inverse analogues (where B is at the terminal position). Isomers of type N-B(R) are found the most stable one among all isomers in both polyene, discussed here. Isomers with both terminal B and N are found of intermediate stability for both BN-polyenes. Highly destabilized isomers are those with one terminal CH_2 group and one terminal heteroatom (B/N) in butadiene series, followed by the one with two terminal CH_2 group, and the isomer with two terminal CH_2 group in hexatriene series, followed by the two isomers with terminal CH_2 group and terminal heteroatom (B/N). Besides structural similarities in these two polyenes, NBO charges observed in the parent iminium ion can also confidently foretell relative thermodynamic stabilities of isomers. Such that the natural charges on iminium ion (N-doped polyene, prior to B-doping) carbons can predict the incoming boron at a particular position, thus leading to an isomer of expected thermodynamic stability.

4. Is It Possible to Hamper Tautomerization of 1H-azirine to 2H-azirine?

Current theoretical study at M06-2X level evaluates electronic, and steric factors to enhance relative thermodynamic stability of 1H-azirine compared to 2H-azirine and hamper its tautomerization to the later.

4.1 Introduction

Azirines, heterocyclic analogues of cyclopropenes, are highly reactive compounds. Azirines are interesting as reactive intermediates in synthetic organic chemistry [40]. They exist in two tautomeric forms: 1H-azirine (**1-H**) comprised of an amine group and a carbon-carbon double bond that readily rearranges to more stable (and sometimes isolable) 2H-azirine (**2-H**) with an imine group and a saturated carbon (Scheme 3.1).



Scheme 4.1: Tautomerization of 1H-azirine (**1-H**) to 2H-azirine (**2-H**).

To best of our knowledge, no 1H-azirine has been isolated yet, since it readily tautomerizes to more stable 2H-azirine [15]. On the other hand, 2H-azirine is not only generated as reactive intermediate but also available through a variety of sources [14]. The instability of 1H-azirines is attributed to the antiaromatic character of the planar ring system with 4π electrons [18]. Thus, any substituent group that can reduce electron density on nitrogen in 1H-azirine can minimize antiaromatic interaction between nitrogen lone pair and ring π -electrons, as a result, can increase its stability [19]. Therefore, accepting this challenging task, we performed DFT investigations to realize the possibility of hampering tautomerization of 1H to 2H-azirine *via* systematic employment of groups of varied electronic and steric nature, not only as migrants on the ring nitrogen but also as substituents on the ring carbons.

4.2 Results and Discussion

4.2.1 Screening of Migrants

Thermodynamic stabilities of 1H-azirines **1** and 2H-azirine **2** are compared in the presence of different migrants and results are summarized in Fig. 4.1. Highly electronegative F group with very weak π -electron donating properties is expected to increase exothermicity of tautomerization (-62.5 kcal/mol), due to unfavored interaction between two highly electronegative atoms in **1-F** (Fig. 4.1) that is also supported by bond dissociation energy (BDE) calculated for B-F bond. Interestingly, BH₂ group is found to stabilize 1H-azirine the most in Fig. 4.1 due to its electron deficient nature that reduces π -electron density on nitrogen indicated by [2p π] natural atomic orbital occupancies (NAOOs) of B and N (0.43 and 1.63 e, respectively). Additionally, planar structure and BDE support BN bond strength higher than all other groups considered in Fig. 4.1. It is worth mentioning here that the NICS(1)_{zz} finds no correlation to the nonplanar 1H-azirines, except for **1-BH₂** that is planar.

Additionally, no correlation to the stabilities of *2H*-azirines (i.e., their $\text{NICS}(1)_{zz}$ hardly change), but stabilities of boryl substituted *1H*-azirines show very good correlation to their $\text{NICS}(1)_{zz}$ values.

	H	CH ₃	SiH ₃	SiF ₃	F	-BH ₂
NICS(1)_{zz}	-7.2	-7.1	0.6	-2.5	-19.0	-0.2
BDE(N-R)	79.6	70.2	64.8	82.5	61.2	104.2
ΔE	-34.7 ↓	-41.0 ↓	-27.8 ↓	-24.6 ↓	-62.5 ↓	-11.4 ↓
NICS(1)_{zz}	-20.0	-19.1	-17.8	-20.2	-22.1	-18.8
BDE(C-R)	113.1	112.2	93.9	107.7	123.4	124.4
ΔBDE	33.5	42.1	29.1	25.2	62.2	20.2

Fig. 4.1: Enthalpies of tautomerization (in kcal/mol) of *1H*-azirine **1** to corresponding *2H*-azirine **2**, and their $\text{NICS}(1)_{zz}$ values (in ppm). $\text{BDE}_{(\text{N-R})}$ and $\text{BDE}_{(\text{C-R})}$ are the bond dissociation energies required to break N-R and C-R bonds, respectively. $\Delta \text{BDE} = \text{BDE}_{(\text{C-R})} - \text{BDE}_{(\text{N-R})}$.

4.2.2 Screening of Substituents

In two separate studies it is found that the boryl (BH_2) migration energy in *1H*-azirine is reduced by σ -electron donating groups at ring carbons (Fig. 4.2a), and use of σ -electron withdrawing substituents at the migrating boron (Fig. 4.2b). The $\text{NICS}(1)_{zz}$ indicates increased aromaticity of *1H*-azirines that might be the reason of their enhanced stability. This increased aromatic character is also depicted by $[2p\pi]$ NAOOs of B and N that rationalize reduced electron density on ring nitrogen within B=N bond (Fig. 4.2b).

(a)				
NICS(1)_{zz}	-4.9	-2.3	4.0	3.2
ΔE	-5.3 ↓	-1.6 ↓	-7.3 ↓	-29.5 ↓
NICS(1)_{zz}	-18.7	-17.3	-19.0	-16.6

(b)				
$[2p\pi]$ NAOO N/B	1.67/0.42	1.57/0.51	1.51/0.60	1.72/0.38
NICS(1)_{zz}	2.4	-1.6	-5.4	0.5
ΔE	-17.3 ↓	-8.1 ↓	0.6 ↓	-24.1 ↓
NICS(1)_{zz}	-20.8	-19.1	-20.0	-21.2

Fig. 4.2: Effect of substituents (at carbons (a) and at boron (b)) on boryl N to C migration. Tautomerization enthalpies are provided in kcal/mol and $\text{NICS}(1)_{zz}$ values in ppm. NAOOs stands for natural atomic orbital occupancies.

4.2.3. Combined Electronic and Steric Effect on Boryl Migration

The best choice migrant $\text{B}(\text{SiF}_3)_2$ (from Fig. 4.2b) is combined with the best choice substituent SiH_3 on carbon (from Fig. 4.2a) in azirine **7** (Scheme 3.2). The tautomerization enthalpy of the resulting *1H*-azirine (**7-SiH₃**) is found significantly endothermic (11.3 kcal/mol). Interestingly, thermodynamic

Degree papers are in the "[Xiamen University Electronic Theses and Dissertations Database](#)". Full texts are available in the following ways:

1. If your library is a CALIS member libraries, please log on <http://etd.calis.edu.cn/> and submit requests online, or consult the interlibrary loan department in your library.
2. For users of non-CALIS member libraries, please mail to etd@xmu.edu.cn for delivery details.

厦门大学博硕士学位论文摘要库