Density Functional Theoretical Investigation on Influence of Heterosubstitution and Benzannelation on the Thermal 6π Electrocyclization of *cis*-Cyclononatetraene

M. Elango and V. Subramanian*

Chemical Laboratory, Central Leather Research Institute, Adyar, Chennai 600 020, India

Received: July 13, 2005; In Final Form: October 26, 2005

Thermal 6π electrocyclization of cyclononatetraene (CNT), its hetero-substituted analogues, and its benzannelated derivatives have been investigated by using the B3LYP method employing 6-31G* and 6-311+G** basis sets. The results indicate that heterosubstitution and benzannelation influence the rate of cyclization. Nucleus independent chemical shifts (NICS), conceptual density functional theory (DFT) based reactivity descriptors, group electronegativity values, and barriers to planarity provide complementary evidence for the predicted rate of cyclization. The available experimental data are in good agreement with the computed values.

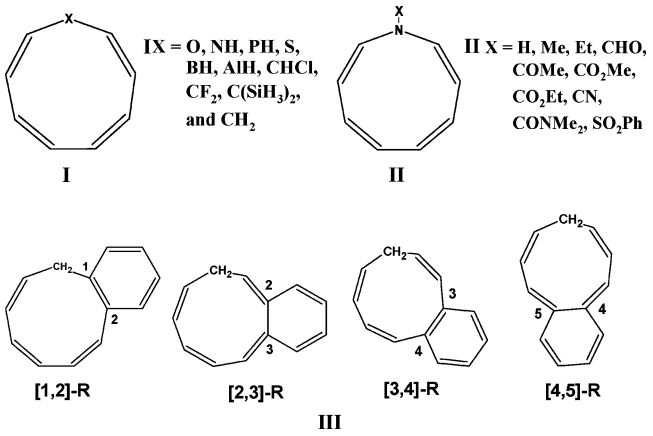
1. Introduction

Heterocycles form one of the largest classical divisions of organic chemistry. Heterocycles play a key role in biochemical processes. The essential constituents of living cells, the majority of pharmaceuticals and biologically active agrochemicals are all heterocycles. Thus, a variety of heterocycles with different structures and properties has been studied using various experimental and theoretical techniques. All the studies have been focused on synthesis, characterization, reactivity and structure of various heterocycles. A special thematic issue in the international chemical journal highlights the multifaceted aspects of heterocycles.[1]

Anastassiou et al. have made seminal contributions to the synthesis and characterization of nine-membered heterocycles, the heteronins (**I**, Chart 1).[2] Heteronins are expected to be aromatic and planar. When warmed to ambient temperature, cyclononatetraene (**IX = CH_2, CNT**) and various thermally labile heteronins rearrange cleanly and exclusively to cis-fused bicyclics.[2a] They exhibit several peculiar properties that make this class of compounds very interesting.[2j] Figure 1 presents different ways by which, heteronin can undergo cyclization into bicyclic forms. Cyclization of (i) a tetraene unit (8π electrons) to a bicyclic [6.1.0] system, (ii) a triene unit (6π electrons) to a bicyclic [4.3.0] system, and (iii) a diene unit (4π electrons) to a bicyclic [5.2.0] system are the allowed thermal and photochemical rearrangements of heteronins. The feasibility of thermal rearrangement of heteronins follow the order 6π cyclization > 4π cyclization > 8π cyclization.

There are few experimental reports on the nine-membered monocyclic molecules[3] in addition to the work of Anastassiou's group. Furthermore, some theoretical studies have also been carried out on oxonin, thionin, and azonin to understand their structure, reactivity and properties.[4] Salcedo et al. investigated the aromaticity of heteronins and also probed into their reactivity with the help of condensed Fukui functions (FF) derived from electronic structure calculations.[5] The aromaticity of various heteronins was analyzed by Schleyer and co-workers using different aromaticity indices.[6] Thermal 6π electrocyclization of heteronins involves a single concerted step that takes place in accordance with Woodward and Hoffmann symmetry rules as given in Figure 2.[7]

CHART 1: General Representation of the Molecules Studied in the Present Work[a]



[a] Nomenclatures used for the annelated CNT are also provided.

To the best of our knowledge a systematic theoretical study on the thermal 6π electrocyclization of the CNT, heterosubstituted analogues of CNT, and benzannelated derivatives of CNT has not been investigated. We present here a DFT(B3LYP) based study of the structure, stability, and electrocyclization of different heteronins. The effect of annelation and heterosubstitution on the cyclization of CNT has been critically investigated.

2. Conceptual DFT Based Reactivity Descriptors

DFT has been quite successful in providing theoretical basis for understanding qualitative chemical concepts introduced to explain chemical reactivity and selectivity. Several global and local reactivity descriptors have been proposed and their utilities in understanding various chemical issues are discussed in the recent reviews.[13] Chemical potential (μ), electronegativity (χ), hardness (η), softness (S), and electrophilicity (ω) are global reactivity descriptors widely used to probe the global reactivity trends. Condensed Fukui function (FF: f_k), local hardness (η_k), local softness (S_k) and local philicity (ω_k) are employed to understand the reactivity at a particular atom. The formal

* Corresponding author. E-mail: subuchem@hotmail.com.

10.1021/jp053860g CCC: $30.25
Published on Web 12/06/2005

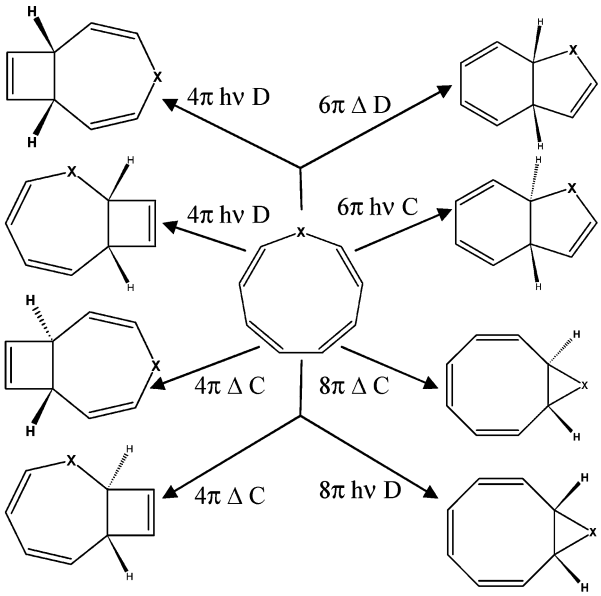


Figure 1. Various thermal (△) and photochemical (hν) rearrangements of heteronins. C: Cis-rotation; D: Dis-rotation.

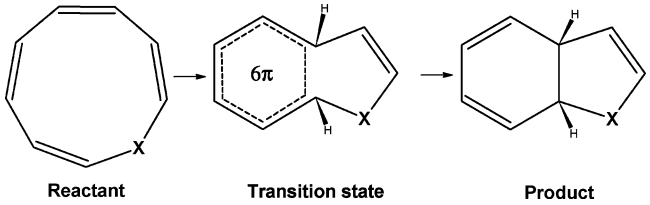


Figure 2. Thermal 6π electrocyclization of nine-membered monocycles to give six- and five-membered bicyclic product.

definitions of various descriptors are provided in the following equations

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{v(\vec{r})} \tag{1}$$

and

$$\chi = -\mu = -\left(\frac{\partial E}{\partial N}\right)_{v(\vec{r})} \tag{2}$$

where $v(\vec{r})$ is the external potential.

Chemical hardness (η) has been identified as useful global reactivity index in atoms, molecules, and clusters. The theoretical definition of chemical hardness has been provided by DFT as the second derivative of electronic energy with respect to the number of electrons (N) for a constant external potential $v(\vec{r})$, viz.,

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\vec{r})} = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right)_{v(\vec{r})} \tag{3}$$

Use of a finite difference method can give the working equations for the calculation of the chemical potential, the electronegativity, and the chemical hardness by

$$\mu = -\frac{\mathrm{IP} + \mathrm{EA}}{2} \chi = \frac{\mathrm{IP} + \mathrm{EA}}{2} \eta = \frac{\mathrm{IP} - \mathrm{EA}}{2} \tag{4}$$

where IP and EA are the ionization potential and electron affinity of the system, respectively.

$$\mathrm{IP} \approx E_{(N-1)} - E_N \quad \text{and} \quad \mathrm{EA} \approx E_N - \mathrm{E}_{(N+1)} \tag{5}$$

where E_N is the electronic energy of the neutral system with N electrons, $E_{(N-1)}$ and $E_{(N+1)}$ are the electronic energy of the species with $N - 1$ and $N + 1$ electrons, respectively.

Parr et al. defined the electrophilicity index,[13c] which measures the stabilization in energy when the system acquires an additional electronic charge, ΔN, from the environment as

$$\omega = \frac{\mu^2}{2\eta} \tag{6}$$

3. Computational Details

It is evident from previous investigations that the B3LYP method provides reliable relative energetics for pericyclic reactions.[8] Hence in this study the same methodology has been adopted. All the structures were fully optimized using the hybrid HF-DFT based B3LYP method using 6-31G* basis set. The optimized reactants and products were characterized as minima on their respective potential energy surfaces by vibrational frequency calculation. Existence of one imaginary frequency was used to characterize the transition sates on their potential energy surface. Further, an intrinsic reaction coordinates (IRC)[9] calculations were carried out to identify its respective reactants and products and also verify the correctness of transition states. The thermodynamic parameters were predicted from the data obtained from the frequency calculations. Reported theromodynamic quantities have been computed at 298.15 K and 1 atm as implemented in G98W. The single point calculations at the B3LYP/6-311+G** level on B3LYP/6-31G* geometries were carried out uniformly for all the species considered in the study. Group electronegativity values were collected from the earlier reports.[10]

The aromaticity of rings was quantified with the help of nucleus independent chemical shifts (NICS) criteria.[11] The NICS(0) is defined as the amount of absolute magnetic shielding calculated at the ring center.[11] Rings with more negative values of NICS are quantified as aromatic by definition, whereas those with positive values are antiaromatic. In this study, we have calculated the NICS(0) value for benzene at the B3LYP/6-31G* level, and this value (−9.7 ppm) is taken as a reference for quantification of aromaticity. Conceptual DFT based reactivity descriptors were calculated using the working equations provided in the previous section. All the calculations were performed using the Gaussian 98 suite of programs.[12] The reactants, the transition states, and the products considered in the study are denoted as **N**−**R**, **N**−**T** and **N**−**P** respectively, where **N** is a general name used to denote each reaction. The same nomenclature has been followed through out.

4. Results and Discussion

The current section is organized as follows. First part describes electrocyclization of CNT and its heterosubstituted analogues (**I**, Chart 1). The second part deals with the effect of replacing H of N in azonine and the cyclization of the resulting molecules (**II**). Cyclization of benzannelated CNT (**III**) and the significance of annelation are discussed in the third part. The usefulness of conceptual DFT descriptors in this study constitutes the last part.

Table 1 presents the calculated activation energies ($\Delta E^{\ddagger}$), enthalpies ($\Delta H^{\ddagger}$), and Gibbs free energies ($\Delta G^{\ddagger}$) of activations for thermal 6π electrocyclization considered in this study. The reaction enthalpies (ΔH_r), energies (ΔE_r) and Gibbs free energies (ΔG_r) of reactions for all the molecules and NICS(0) values for the reactants are summarized in Table 2. It is evident from Table 1 that activation energies and free energies of activation

TABLE 1: Activation Enthalpies ($\Delta H^{\ddagger}$), Energies ($\Delta E^{\ddagger}$), and Gibbs Free Energies ($\Delta G^{\ddagger}$) of Activations Obtained at the B3LYP/6-31G* Level and Activation Energies Obtained at the B3LYP/6-311+G Level for the 6π Thermal Electrocyclization of All of the Molecules[a]**

species	$\Delta H^{\ddagger}$	$\Delta G^{\ddagger}$	$\Delta E^{\ddagger}$	$\Delta E^{\ddagger}$ [b]
O	20.63 (18.20)[2a]	22.20	22.41	22.57
NH	29.67	30.88	33.22	33.18
PH	18.41	19.81	19.48	19.96
S	21.00	22.63	22.27	22.79
BH	14.45	16.06	15.57	16.50
AlH	21.33	23.44	22.43	23.09
CHCl	18.02	19.69	19.47	20.01
CF_2	18.63	19.72	19.84	20.55
$C(SiH_3)_2$	20.81	21.63	22.38	23.10
CNT	20.08 (19.80)[2a]	21.55 (22.90)[2g]	21.58	22.22
[1,2]	19.63	21.18 (22.40)[2g]	20.86	21.93
[2,3]	5.75	7.10	7.43	7.49
[3,4]	32.20	33.57	33.93	35.04
[4,5]	5.79	6.87	6.97	7.54
NMe	26.24	28.80	29.48	30.18
NEt	28.42	29.93	31.73	32.14
NCHO	21.66	23.06	23.42	23.81
NCOMe	21.31 (23.40)[2a]	22.62	22.77	23.54
NCO_2Me	21.85	22.88	23.32	23.72
NCO_2Et	21.86 (21.20)[2a]	22.84	23.37	23.79
NCN	21.36	23.36	23.06	23.62
$NCONMe_2$	23.38 (24.80)[2a]	24.96	25.14	26.03
NSO_2Ph	21.98 (22.30)[2a]	23.31	23.53	24.17

[a] All values are in kcal/mol. Values in parentheses are corresponding experimental data. [b] Obtained from single-point B3LYP/6-311+G** calculations done on B3LYP/6-31G* geometries.

TABLE 2: Reaction Enthalpies (ΔH_r), Energies (ΔE_r), and Gibbs Free Energies (ΔG_r) of Reactions Obtained at the B3LYP/6-31G* Level and NICS(0) Values of the Nine-Membered Ring Obtained at the B3LYP/6-31G* Level and Reaction Energies Obtained at the B3LYP/6-311+G Level for the 6π Thermal Electrocyclization of All of the Molecules[a]**

species	ΔH_r	ΔG_r	ΔE_r	ΔE_r[b]	NICS(0) (ppm)
O	−22.35	−20.83	−22.75	−20.83	−4.2
NH	−11.44	−9.10	−9.45	−9.10	−13.6
PH	−27.71	−25.96	−28.76	−25.96	1.1
S	−26.44	−24.52	−27.43	−25.85	−0.5
BH	−20.90	−19.63	−21.64	−19.63	1.7
AlH	−16.31	−14.57	−17.24	−14.57	1.2
CHCl	−24.32	−22.76	−24.92	−22.76	3.5
CF_2	−25.20	−22.68	−25.51	−22.68	0.5
$C(SiH_3)_2$	−22.56	−21.25	−23.08	−21.25	−1.4
CNT	−22.61	−21.14	−23.13	−21.14	2.7
[1,2]	−24.06	−22.48	−24.77	−22.48	1.9
[2,3]	−51.56	−49.85	−52.15	−49.85	11.3
[3,4]	−1.12	0.08	−1.26	0.08	1.4
[4,5]	−52.43	−50.31	−53.59	−50.31	2.1
NMe	−14.99	−12.75	−13.86	−12.75	−12.4
NEt	−13.49	−11.93	−12.29	−11.93	−12.5
NCHO	−21.96	−20.65	−22.30	−20.65	−3.1
NCOMe	−20.32	−19.37	−21.02	−19.37	0.1
NCO_2Me	−22.57	−21.75	−23.22	−21.75	−0.7
NCO_2Et	−22.51	−21.74	−23.14	−21.74	−0.7
NCN	−21.94	−20.03	−22.32	−20.03	−4.0
$NCONMe_2$	−18.03	−16.12	−18.26	−16.12	−3.6
NSO_2Ph	−20.15	−18.67	−20.70	−18.67	−1.5

[a] All the values are in kcal/mol. [b] Obtained from single-point B3LYP/6-311+G** calculations done on B3LYP/6-31G* geometries.

follow the activation enthalpies, and thus, the activation enthalpies are taken for discussion. It can be observed from Table 1 that the activation enthalpies[2a] and free energies[2g] predicted at the B3LYP/6-31G* level of calculation are in close agreement with the available experimental values. The optimized geometrical structures of all the reactants and transition states are collected in Figures 3 and 4, respectively. Since, the rate of cyclization depends strongly on initial geometries of the reactants; geometries of reactants are analyzed to obtain expected correlation.

4.1. Heterosubstituted CNT. NH, O, PH, S, BH, AlH, CF_2, CHCl, and $C(SiH_3)_2$ are the substituents used to study the effect of hetero-substitution on cyclization of **I**. Among the substituted molecules, **NH−R**, **O−R**, **PH−R**, and **S−R** are 10π electron systems and **BH−R**, **AlH−R**, **CF_2−R**, **CHCl−R**, and **C-$(SiH_3)_2$−R** are 8π electron systems. **CNT−R** is a structurally distorted molecule with 8π electrons. The NICS(0) value for CNT-R is 2.7 ppm. Comparison of this NICS(0) value with that of benzene suggests that it is antiaromatic in nature. The barrier for the cyclization of **CNT−R** to **CNT−P** through **CNT−TS** is 20.1 kcal/mol. The cyclization of **CNT−R** has been calculated to be exothermic by 22.6 kcal/mol. In the discussion, the activation enthalpy and reaction enthalpy calculated for cyclization of **CNT−R** has been taken as the reference value to study the effect of heterosubstitution and benzannelation.

Azonin (**IX = NH**, **NH−R**) has a planar geometry and the planarity is due to the delocalization of lone pair on nitrogen over the entire ring. **NH−R** has more aromatic character as evident from its NICS(0) value of −13.6 ppm when compared to that of **CNT−R**. For the cyclization of **NH−R**, the activation enthalpy is predicted to be 29.7 kcal/mol. To undergo cyclization, **NH−R** has to sacrifice its aromaticity and as a result high activation enthalpy has been observed for its cyclization. The formation of **NH−P** is less exothermic than that for **CNT−P** by 11 kcal/mol. Thus, the cyclization of **NH−R** to **NH−P** is not feasible in comparison with that of **CNT−R** to **CNT−P**. Oxonin (**IX = O**, **O−R**) exhibits a nonplanar structure. The nonplanarity of **O−R** can be attributed to the strong electron localizing effect of oxygen. The NICS(0) value for **O−R** is 4.2 ppm, and therefore it is antiaromatic in nature. The rearrangement of **O−R** to **O−P** proceeds with a barrier of 20.63 kcal/mol and is exothermic by 22.35 kcal/mol. It is clear from the results that O substitution has no significant effect on cyclization of **O−R** compared to **CNT−R**.

Thionin (**IX = S**, **S−R**) has not yet been synthesized, and all of the attempts to synthesize this molecule ended up in different molecules.[2a] The minimum energy structure of **S−R** is a distorted geometry and this observation is in line with a recent study.[6] The NICS(0) value for **S−R** is −0.5 ppm. Therefore, it is not aromatic. The cyclization of **S−R** via **S−TS** has a barrier of 21.0 kcal/mol. The formation of **S−P** is exothermic by 26.44 kcal/mol. These results suggest that S substitution has a minor effect on cyclization of **S−R** compared to **CNT−R**. Phosphonin (**IX = PH**, **PH−R**) is antiaromatic molecule as seen from its NICS(0) value of 1.1 ppm. The activation barrier for the cyclization of **PH−R** is about 2 kcal/mol less than that for **CNT−R**. The formation of **PH−P** is 5 kcal/mol more exothermic as compared to **CNT−P**. Hence, PH substitution decreases the activation barrier and increases the reaction exothermicity for cyclization of **PH−R** compared to **CNT−R**.

Boronin (**IX = BH**, **BH−R**) has 8π electrons. The NICS(0) value for **BH−R** is 1.7 ppm, which means that it is anti aromatic in nature. The minimum energy structure is a highly distorted geometry. The concerted closure of **BH−R** to **BH−P** proceeds with a barrier of 14.5 kcal/mol and is exothermic by 20.9 kcal/mol. As compared to that for **CNT−R**, the barrier calculated for the cyclization of **BH−R** has been lowered by 6 kcal/mol. Therefore, BH substitution facilitates the cyclization of **BH−R** compared to **CNT−R**. **AlH−R** (**IX = AlH**) is an 8π electron

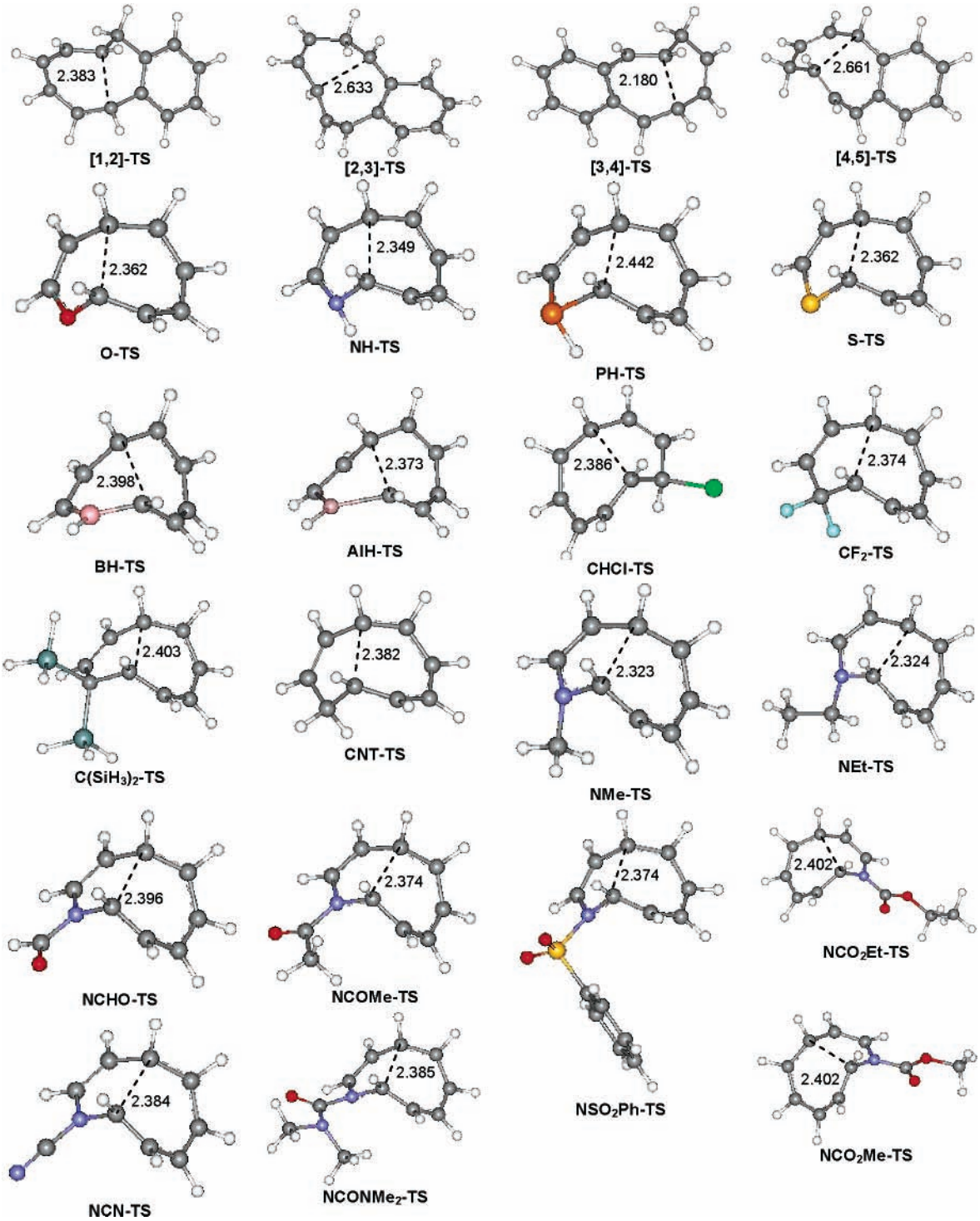


Figure 3. B3LYP/6-31G* optimized geometries of the transition states of all the reactions. The bond lengths are given in Å.

system. Its NICS(0) value (1.2 ppm) reveals that it is anti aromatic. The cyclization of **AlH**−**R** to **AlH**−**P** has been calculated to have activation enthalpy of 21.33 kcal/mol. The formation of **AlH**−**P** has been calculated to be exothermic by 16.3 kcal/mol, which is 6 kcal/mol less exothermic than that of **CNT**−**P**. Therefore, AlH substitution do not favor cyclization of **AlH**−**R** when compared to **CNT**−**R**.

With a view to understand the role of hyperconjugation and their effect on cyclization, CF_2, CHCl, and $C(SiH_3)_2$ substitution have been included in this investigation. The NICS(0) value for **CF_2**−**R**, **CHCl**−**R**, and **$C(SiH_3)_2$**−**R** are +0.5, +3.5, and −1.4 ppm, respectively. This indicates that the first two reactants are antiaromatic and the last one is less aromatic. The barriers calculated for the cyclization of **CF_2**−**R** and **CHCl**−**R** to **CF_2**−**P** and **CHCl**−**P** has been lowered by 2 kcal/mol compared to that for **CNT**−**R** to **CNT**−**P**. And also, the formation of **CF_2**−**P** and **CHCl**−**P** are more exothermic by 3 kcal/mol than that for **CNT**−**P**. In the case of **$C(SiH_3)_2$**−**R** the activation barrier for cyclization is 20.81 kcal/mol. The formation of **$C(SiH_3)_2$**−**P** is exothermic by 22.56 kcal/mol. It is clear from these results that CF_2, CHCl substitution favor the cyclization of **CF_2**−**R** and **CHCl**−**R** whereas $C(SiH_3)_2$ substitution does not have any effect on the cyclization of **$C(SiH_3)_2$**−**R**, compared to **CNT**−**R**.

4.2. N-Substituted Azonins. It is evident from the calculations that azonin is planar and more aromatic in nature. An

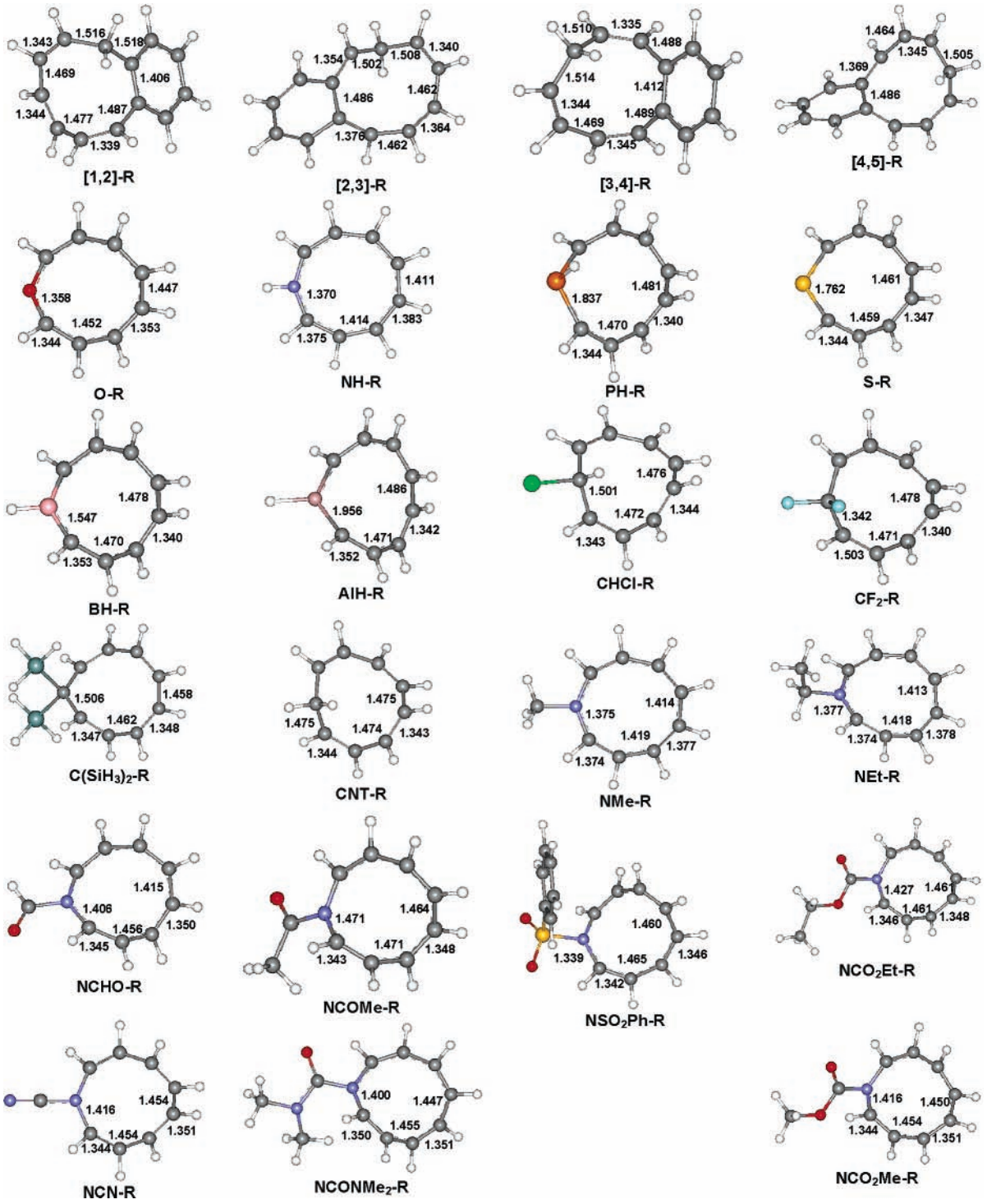


Figure 4. B3LYP/6-31G* optimized geometries of the reactants of all the reactions. The bond lengths are given in Å.

attempt has been made to replace H of N in azonin with various groups ranging from electron withdrawing to electron releasing and to study the feasibility of cyclization in the resulting molecules (**II**). The different groups chosen for the attempt includes CH_3, C_2H_5, CHO, COMe, COOMe, COOEt, CN, $CONMe_2$, and SO_2Ph. The NICS(0) value for all the species indicates that, except for **NEt-R** and **NMe-R**, all are nonaromatic in nature. The optimized molecular structures show that planarity is lost in all the molecules with the exception of **NEt-R** and **NMe-R**. It should be mentioned here that the lone pair on nitrogen atom is not completely available for the cyclic delocalization, and as a result planarity and aromaticity is lost. This is reflected in the faster rate of cyclization of N-substituted azonines compared to azonine itself. The activation enthalpy for cyclization is lowered by 5 kcal/mol and the cyclization is more exothermic by 6 kcal/mol compared to azonine. There is little effect on the rate of cyclization of **NEt-R** and **NMe-R** when compared to azonine.

The loss of planarity has been quantified by measuring the barriers to planarity. The difference ($E_{planarity} = E_A^* - E_A$) in the energies of minimum geometry (E_A) and planar geometry (E_A^*) for the same molecule is taken as its barriers to planarity ($E_{planarity}$). Here, the planar geometry is obtained by imposing geometrical constraints whereas minimum geometry is allowed to optimize freely. An attempt has been made to relate barriers to planarity, electronegativity values of the groups chosen, and

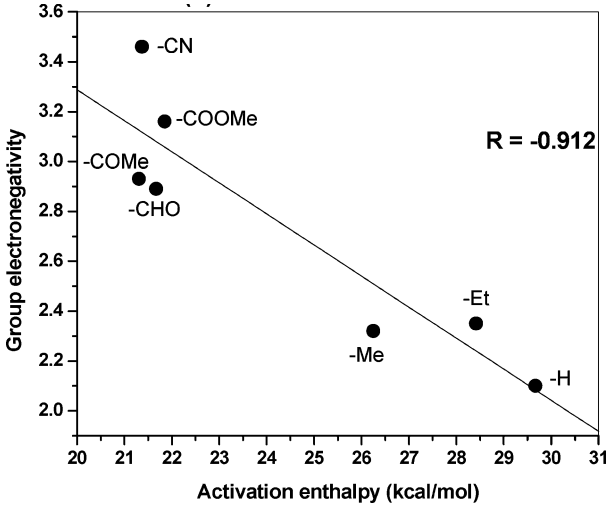


Figure 5. Linear plot between group electronegativity and activation enthalpy of cyclization for the class of N-substituted azonines.

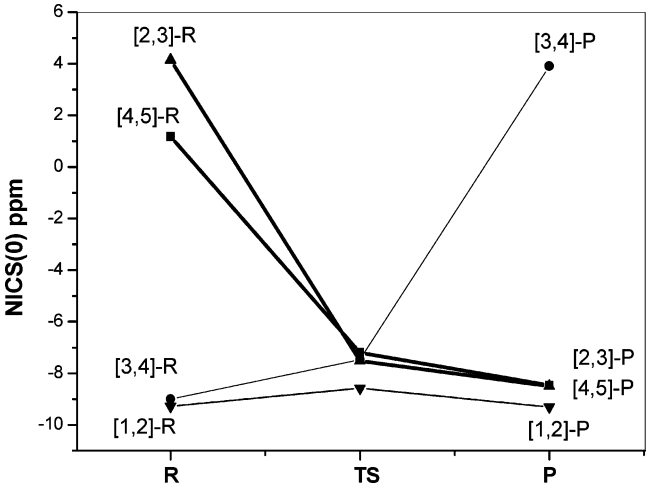


Figure 6. Variation of NICS(0) values of the annelated benzene ring in reactant (R), transition state (TS) and product (P).

activation enthalpy for cyclization. In the development of relationship, groups with known experimental electronegativity values have been used. It could be seen from Figure 5 that group electronegativity exhibits an inverse relationship with activation enthalpy. The correlation ($R = -0.912$) indicates a reasonable relation between activation enthalpy and electronegativity. However, the relationship between barriers to planarity and activation enthalpy is not satisfactory.

4.3. Benzannelated CNT. It has been reported in the earlier studies that annelation can reduce the barrier for cyclization.[14] In this context, it is worth investigating the effect of benzannelation on the cyclization of CNT. It is possible to obtain four different isomers from benzannelation of CNT (**III**). Activation and reaction parameters have been calculated for cyclization of all the isomers and are compared with **CNT−R**.

It is interesting to note that cyclization of **[2,3]-R** and **[4,5]-R** are highly feasible with lower activation enthalpies of 5.75 and 5.79 kcal/mol, respectively. The cyclizations of **[2,3]-R** and **[4,5]-R** have been the most exothermic processes studied (51.56 and 52.43 kcal/mol, respectively). It should be noted that the geometrical structures of **[2,3]-R** and **[4,5]-R** have a quinodimethane part. Quinodimethanes are highly reactive intermediates[15] and they facilitate the faster cyclization of **[2,3]-R** and **[4,5]-R** to **[2,3]-P** and **[4,5]-P**. The highest activation barrier, of 32.20 kcal/mol, has been observed for the cyclization of **[3,4]-R** to **[3,4]-P**. The cyclization of **[3,4]-R** is the least exothermic process studied (1.12 kcal/mol). Interestingly the cyclization of **[1,2]-R** to **[1,2]-P** is calculated to have a similar activation barrier and exothermicity as those for the **CNT−R** to **CNT−P** reaction. The reason is that the annelated portion of CNT does not participate in the cyclization.

There are several attempts to relate the aromaticity of molecules to its reactivity. To obtain relation between aromaticity and cyclization in benzannelated systems, NICS(0) index has been computed along the reaction coordinate. Variation of aromatic behavior of the annelated benzene ring along the reaction coordinate is plotted in Figure 6. It is evident from the figure that, annelated benzene ring in isomers **[2,3]-R** and **[4,5]-R** gain aromaticity when going from reactants to transition states to products. As a result the calculated activation barrier is abruptly reduced. However, in the case of **[3,4]-R**, the aromaticity of the benzene is lost along the reaction coordinate. Therefore, the cyclization barrier for **[3,4]-R** is high. Interestingly, there is little change in the aromatic nature of annelated benzene in **[1,2]-R**. The NICS(0) values along the reaction coordinate clearly support the observed rate of cyclization. Similar observation has also been pointed out by Zora et al.[16] in their recent studies that gain in aromaticity in the course of forming the transition structures lowers the barrier for cyclization.

TABLE 3: Chemical Hardness (η) and Electrophilicity (ω) Values for All of the Reactants Calculated at the B3LYP Level of Theory Using the 6-31G* Basis Set

reactants	η (eV)	ω (eV)
O−R	4.62	1.14
NH−R	4.21	1.06
PH−R	4.46	1.31
S−R	4.35	1.09
BH−R	4.18	2.03
AlH−R	4.05	1.89
CHCl−R	4.05	1.78
CF_2−R	4.57	1.58
$C(SiH_3)_2$−R	4.44	1.19
CNT-R	4.32	1.29
[1,2]-R	4.41	1.27
[2,3] −R	2.93	1.99
[3,4]-R	4.36	1.27
[4,5] −R	3.28	1.69
NMe-R	4.16	1.05
NEt-R	4.13	1.04
NCHO−R	4.28	1.38
NCOMe-R	4.16	1.26
NCO_2Me-R	4.25	1.13
NCO_2Et-R	4.23	1.12
NCN−R	4.35	1.42
$NCONMe_2$−R	4.11	1.15
NSO_2Ph-R	3.78	1.59

4.4. Chemical Reactivity Descriptor Analysis. The computed values of global reactivity parameters for all the reactants are listed in Table 3. Stability and reactivity of the molecules are analyzed with the help of chemical hardness (η) and electrophilicity (ω) values. A molecule with more η value is found to be more stable and less reactive. On the other hand a molecule with more ω is said to be more reactive and less stable. The calculated DFT reactivity descriptors for heterosubstituted systems clearly show that electrophilicity values are able to predict the reactivity trend as observed using activation parameters. On the basis of the electrophilicity values **NH−R** (1.06 eV) is found to be least reactive whereas **BH−R** (2.03 eV) is highly reactive among heterosubstituted CNT. This is in agreement with the activation parameters calculated for cyclization. In the case of N-substituted azonines, **NH−R** (1.06

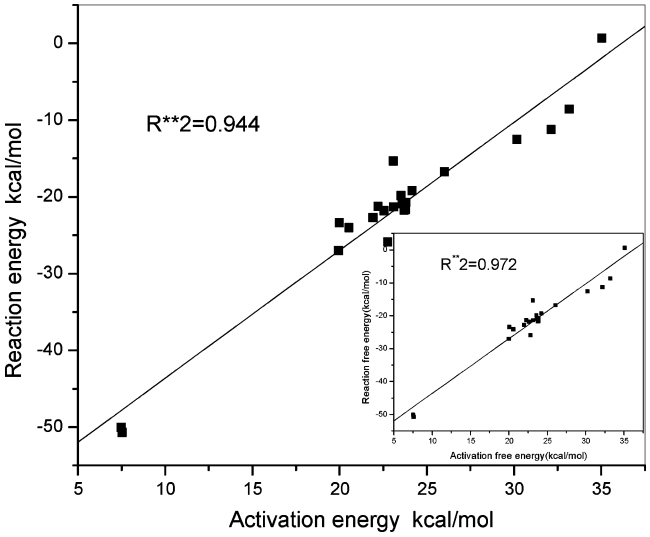


Figure 7. Relationship between activation and reaction parameters for all the reaction.

eV), **NMe-R** (1.05 eV), and **NEt-R** (1.04 eV) are the least reactive molecules as observed from the electrophilicity values. Other molecules in the category are more reactive and hence cyclization is faster when compared to **NH**−**R**, **NMe-R**, and **NEt-R**. In the case of benzannelated isomers, **[2,3]-R** and **[4,5]-R** are the least stable molecules with hardness values of 2.93 and 3.28 eV, respectively. The electrophilicity values are more comparable to other isomers (1.99 and 1.69 eV, respectively) and hence they exhibit high potential for cyclization. Isomers **[1,2]-R** and **[3,4]-R** are less reactive with hardness values 4.41 and 4.36 eV, respectively, and therefore they undergo cyclization slowly. It is important to point out here that both hardness and electrophilicity values could yield reactivity of the most and least reactive species. Nevertheless, it is not possible to obtain reactivity trend for the entire series of molecules. The range within which, the activation parameters for the cyclization of some of the reactants fall is very less. Similarly, the differences in the values of the reactivity descriptors are also very small. Approximations used in the calculation of reactivity descriptors and the level of calculation may influence the numerical values. As a consequence, it may not be possible to obtain the trend in accordance with the activation parameters. The plot between reaction and activation energies calculated for the cyclization of all the molecules is shown in Figure 7. From the linear relationship, it is clear that faster the rate of cyclization, the more stable is the product formed.

5. Conclusions

In the present study thermal 6π electrocyclization of CNT, various heteronins and benzene-fused CNT has been analyzed at the B3LYP/6-31G* level of theory. The following conclusions emerge from the calculations. Azonine does not favor cyclization and also requires high activation energy due to its aromatic character and planarity. Boronin favors cyclization when compared to that of all other heterosubstituted analogues. O substitution does not significantly impart effects on the cyclization. CF_2 and CHCl favor cyclization due to hyperconjugation. Replacing H of N in azonine influences the aromaticity and hence rate of cyclization. Both barrier to planarity and group electronegativity displays linear relationship with activation enthalpy in the case of substituted azonines. In the case of benzannelated CNT, the extent of cyclization is strongly influenced by the position of annelation**.** It is possible to note that [2,3] and [4,5] positions favor cyclization and [3,4] does not support cyclization. Benzannelation at the [1,2] position does not have any effect on cyclization when compared to CNT. The linear relationship between activation and reaction parameters indicates that a faster cyclization results in a stabler product.

Acknowledgment. We are thankful to the CSIR, New Delhi, for financial assistance.

Supporting Information Available: Figures showing optimized structures of products and thermochemical data, tables of total energies and optimized Cartesian coordinates for all the reactants, transition states, and products obtained at the B3LYP/6-31G* level, and text giving the details of calculation of NICS (with a table of input values) using the Gaussian 98W package. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Katritzky, A. R. *Chem. Rev.* **2004**, *104*, 2125.

(2) (a) Anastassiou, A. G. *Acc. Chem. Res.* **1972**, *5*, 281. (b) Anastassiou, A. G.; Eachus, S. W.; Cellura, R. P.; Gebrian, J. H. *J. Chem. Soc., Chem. Commun.* **1970**, 1133. (c) Anastassiou, A. G.; Gebrian, J. H. *J. Am. Chem. Soc.* **1969**, *91*, 4011. (d) Anastassiou, A. G.; Cellura, R. P. *J. Chem. Soc., Chem. Commun.* **1969**, 903. (e) Anastassiou, A. G.; Cellura, R. P. *J. Chem. Soc., Chem. Commun.* **1969**, 1521. (f) Anastassiou, A. G.; Cellura, R. P.; Gebrian, J. H. *J. Chem. Soc. Chem. Commun.* **1970**, 375. (g) Anastassiou, A. G.; Griffith, R. C. *J. Am. Chem. Soc.* **1974**, *96*, 611. (h) Anastassiou, A. G.; Reichmanis, E. *J. Am. Chem. Soc.* **1976**, *98*, 8266. (i) Anastassiou, A. G.; Libsch, S. S.; Griffith, R. C. *Tetrahedron Lett.* **1973**, *14*, 3103. (j) Anastassiou, A. G. *Pure Appl. Chem.* **1975**, *44*, 691.

(3) (a) LaLancette, E. A.; Benson, R. E. *J. Am. Chem. Soc.* **1965**, *87*, 1941. (b) Lombardo, L.; Wege, D. *Tetrahedron* **1974**, *30*, 3945. (c) Baldwin, J. E.; Andrist, A. H.; Pinschmidt, R. K. *J. Am. Chem. Soc.* **1972**, *94*, 5845. (d) Berson, J. A.; Boettcher, R. R.; Vollmer, J. J. *J. Am. Chem. Soc.* **1971**, *93*, 1540. (e) Hess, B. A.; Schaad, L. J., Jr.; Holyoke, C. W., Jr. *Tetrahedron* **1972**, *28*, 3657.

(4) (a) Hess, B. A.; Schaad, L. J., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 3907. (b) Mukherjee, N. G. *Indian J. Chem. B* **1994**, *33*, 87. (c) Ouamerali, O.; Gayoso, J. *Int. J. Quantum Chem.* **1986**, *29*, 1599. (d) Aihara, J. *J. Am. Chem. Soc.* **1976**, *98*, 2750. (e) Juric, A.; Sabljic, A.; Trinajstic, N. *J. Heterocycl. Chem.* **1984**, *21*, 273. (f) Somers, K. R. F.; Kryachko, E. S.; Ceulemans, A. *J. Phys. Chem. A* **2004**, *108*, 4059.

(5) Salcedo, R.; Martinez, A.; Sansores, L. E. *Tetrahedron* **2001**, *57*, 8759.

(6) Schleyer, P. v. R.; Nyulászi, L.; Kárpáti, T. *Eur. J. Org. Chem.* **2003**, *2003*, 1923.

(7) Woodward, R. B.; Hoffmann, R. *Angew Chem., Int. Ed. Engl.* **1969**, *8*, 781.

(8) (a) Wiest, O.; Montiel, D. C.; Houk, K. N. *J. Phys. Chem. A* **1997**, *101*, 8378. (b) Goldstein, E.; Beno, B. R.; Houk, K. N. *J. Am. Chem. Soc.* **1996**, *118*, 6036. (c) Guner, V.; Khuong, K. S.; Leach, A. G.; Lee, P. S.; Bartberger, M. D.; Houk, K. N. *J. Phys. Chem. A* **2003**, *107*, 11445. (d) Hrovat, D. A.; Chen, J.; Houk, K. N.; Borden, W. T. *J. Am. Chem. Soc.* **2000**, *122*, 7456. (e) Houk, K. N.; Beno, B. R.; Nendel, M.; Black, K.; Yoo, H. Y.; Wilsey, S.; Lee, J. K. *J. Mol. Struct. (THEOCHEM)* **1997**, *398*, 169. Sperling, D.; Reissig, H. U.; Fabian, J. *Liebigs Ann. Recl.* **1997**, 2443. (f) Ozkan, I.; Zora, M. *J. Org. Chem.* **2003**, *68*, 9635.

(9) Ishida, K.; Morokuma, K.; Komornicki, A. *J. Chem. Phys.* **1977**, *66*, 2153.

(10) (a) Marriott, S.; Reynolds, W. F.; Taft, R. W.; Topsom, R. D. *J. Org. Chem.* **1984**, *49*, 959. (b) Mullay, J. *J. Am. Chem. Soc.* **1985**, *107*, 7, 7271. (b) Boyd, R. J.; Edgecombe, K. E. *J. Am. Chem. Soc.* **1988**, *110*, 4182. (c) Boyd, R. J.; Boyd, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 1652. (d) De Proft, F.; Langenaeker, W.; Geerlings, P. *J. Phys. Chem.* **1993**, *97*, 7, 1826.

(11) (a) Mauksch, M.; Gogonea, V.; Jiao, H.; Schleyer, P. v. R. *Angew. Chem., Int. Ed.* **1998**, *37*, 2395. (b) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. R. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317. (c) Subramanian, G.; Schleyer, P. v. R.; Jiao, H. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2638. (d) Schleyer, P. v. R.; Manoharan, M.; Wang, Z. X.; Kiran, B.; Jiao, H.; Puchta, R.; Hommes, N. J. R. v. E. *Org. Lett.* **2001**, *35*, 2465. (e) Schleyer, P. v. R.; Manoharan, M.; Jiao, H.; Stahl, F. *Org. Lett.* **2001**, *35*, 3643.

(12) Frisch, M. J.; et al. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(13) (a) Geerlings, P.; De Proft, F.; Langenaeker, W. *Chem. Rev.* **2003**, *103*, 1793. (b) Chermette, H. *J. Comput. Chem.* **1999**, *20*, 129. (c) Parr, R. G.; Szentpaly, L. v.; Liu, S. *J. Am. Chem. Soc.* **1999**, *121*, 1922.

(14) (a) Dinadayalane, T. C.; Punnagai, M.; Sastry, G. N. *J. Mol. Struct. (THEOCHEM)* **2003**, *626*, 247. (b) Alabugin, I. V.; Manoharan, M. *J. Am. Chem. Soc.* **2003**, *125*, 4495. (c) Prall, M.; Wittkopp, A.; Schreiner, P. R. *J. Phys. Chem. A* **2001**, *105*, 9265. (d) Laali, K. K.; Rasul, G.; Surya Prakash, G. K.; Olah, G. A. *J. Org. Chem.* **2002**, *67*, 2913. (e) Alabugin, I. V.; Manoharan, M.; Kovalenko, S. V. *Org. Lett.* **2002**, *4*, 1119.

(15) Manoharan, M.; De Proft, F.; Geerlings, P. *J. Org. Chem.* **2000**, *65*, 7971.

(16) (a) Zora, M. *J. Org. Chem.* **2004**, *69*, 1940. (b) Zora, M. *J. Org. Chem.* **2004**, *69*, 857.