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# Computational Chemistry Methods

Applications Edited by Ponnadurai Ramasami

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# Preface

A virtual conference on computational science (VCCS-2018) was organized online from 1<sup>st</sup> to 31<sup>st</sup> August 2018. This was the sixth virtual conference which was started in 2013. The month of August was chosen to commemorate the birth anniversary of Erwin Schrödinger, the father of quantum mechanics, on 12<sup>th</sup> August.

There were 30 presentations for the virtual conference with 100 participants from 20 countries. A secured platform was used for virtual interactions of the participants. After the virtual conference, there was a call for full papers to be considered for publication in the conference proceedings. Manuscripts were received and they were processed and reviewed as per the policy of De Gruyter.

This book is a collection of the eight accepted manuscripts based on the use of computational chemistry methods. These manuscripts cover a range of topics from fundamental to applied science. Choong et al investigated the conformations and interactions between *R*- and *S*-methandone in wild type CYP2B6, 2D6 and 3A4. Gümüş et al studied the aromaticity of mono, di, tri and tetraazaphenantherene derivatives. Renita and Sivasubramanian reviewed the application of computational chemistry for adsorption studies on metal organic frameworks for carbon capture. Kuznetsov performed a DFT study on phthalocyanines core-modified by P and S and their complexes with C60. Kharkar et al presented models for the computational predication of toxicity of small organic molecules. Kakkar et al reviewed a combined approach of homology modeling, molecular dynamics and docking towards computer-aided drug discovery. Ramasami et al investigated the structural and spectroscopic parameters of 2,4-dichloro-N-phenethylbenzenesulfonamide and 2,4-dimorpholino-4-yl-6-(4-nitrophenoxy)-[1,3,5]-triazine in combined experimental and DFT studies.

I hope that these chapters will add to literature and they will be useful references.

To conclude, VCCS-2018 was a successful event and I would like to thank all those who have contributed. I would also like to thank the Organising and International Advisory committee members, the participants and the reviewers.

Prof. Ponnadurai Ramasami

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Erhan Öztürk, Zeynep Turhan İrak, Necdet Karakoyun, Ayşegül Gümüş and Selçuk Gümüş

# 1 Investigation of the aromaticity of mono, di, tri and tetraazaphenanthrene derivatives

**Abstract:** In this chapter mono, di, tri and tetraaza substituted phenanthrene derivatives have been investigated computationally with B3LYP/6-31 + G(d,p) level of theory. Substitution of carbon atom of the main structure with nitrogen obviously disturbs the aromaticity, indeed it decreases it. Thus, the idea of regaining of the aromaticity back by using electron withdrawing groups came across. As a result of the computational calculations, energetically most unfavored structures have been found to be those where aza substitutiona are vicinal. Secondly, the aromaticities of the present species depend on the position of the centric substituent. In addition, the effect position of the side substituent has been considered. The system becomes more aromatic (possess greater negative NICS values or smaller HOMA value) when the electron withdrawing atoms or groups are adjacent to the centrically substituted heteroatoms.

Keywords: aromaticity, NICS, HOMA, phenanthrene, azaphenanthrene

## **1.1 Introduction**

The polycyclic aromatic hydrocarbon formed by fusing three benzene rings is called Phenanthrene (**Ph**) which takes its name from two well-known chemical compounds; 'phenyl' and 'anthracene'. is It has a role as an environmental contaminant and a mouse metabolite. It is an ortho-fused polycyclic arene, an ortho-fused tricyclic hydrocarbon and a member of phenanthrenes (Figure 1.1). The steroids possess phenanthrene in their framework. It is a harmfull material in its pure form, which is spread out by cigarette smoke. Its irritant and photosensitising skin to light properties are well known. Phenanthrene emerges as a white powder chemical emitting blue fluorescence. Although is insoluble in water its solubility in most organic solvents, including toluene, carbon tetrachloride, ether, chloroform, acetic acid and benzene, is quite high. Bardhan-Sengupta Phenanthrene Synthesis is the classical synthetic application to obtain **Ph** [1].

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Figure 1.1: Structure of phenanthrene and naming of the rings.



Figure 1.2: Resonance structures of phenanthrene.

Phenanthrene has a significant resonance stabilization due to its tricyclic aromatic structure, as shown in the following diagram (Figure 1.2). Three fused benzene ring moieties is one of the five contributing resonance structures, in two of the structures  $10 \pi$ -electron annulene is fused to a benzene ring, and the remaining two geometries are  $14 \pi$ -electron annulenes. All of the resonans structures are aromatic by the https://www2.chemistry.msu.edu/faculty/reusch/virttxtjml/react3. htm#rx9ac Hückel Rule. A careful inspection of each contributing structure reveals that the carbon-carbon bond of the B–Ring has 80 % double bond character (1.34 Å bond length), whereas the opposite bond across the circle has 80 % single bond character with 1.47 Å bond length. The bond lengths shown on the right hand structure reflected that the other carbon-carbon bonds vary in terms of bond order. As expected, the carbon–carbon bonds with more than 80 % double bond character, display double bond-like addition reactions, including simple catalytic hydrogenation. Indeed both radical and polar addition reactions are observed by all the aromatic fused ring compounds which less readily benzene undergoes.

Kalescky et al. [2] introduced a new description for the aromaticity of polycyclic compounds including phenantherene. They compared the aromatic character of the compounds in terms of bond strengths obtained from computations of vibrational frequencies. A similar argument was concluded for phenanthrene since the bond with double bond character was calculated to be much more stronger than the bond with single bond character [2].

Apart from the **Ph** itself azaphenanthrene derivatives have been considered by the researchers both experimentally and theoretically [3–7]. The most popular

azaphenanthrene in the literature is 1,10-phenanthroline [7]. 1,10-Phenanthroline (**Ph\_1\_10**) took part very important role in the development of coordination chemistry due to being a classic chelating bidentate ligand for transition metal cations [8–10]. Considerable interest to it as adaptable starting material for organic, inorganic and supramolecular chemistry still continues. **Ph\_1\_10** possess rigid planar, hydrophobic, electron-poor heteroaromatic character whose nitrogens are located nicely to act together in cation coordination. Thus, its binding ability toward metal ions is determined by these structural features [9, 10].

Research on aromaticity has still been an intensively investigated area of chemistry. The Huckel rule states that; if monocyclic aromatic compounds with cyclic conjugated  $\pi$ -systems contain the proper number of  $\pi$ -electrons, they are considered to be aromatic. Although these criteria are strong enough to decide the aromaticity of neutral and charged ring systems, some additional definitions are necessary to indicate the aromaticity of more complex systems clearly (as in our case).

In general, aromaticity can be expressed by a combination of terms such as energetic, structural and magnetic criteria in cyclic delocalized systems [11–16]. Nucleus-Independent Chemical Shift (NICS) has been introduced by Schleyer in 1996, which is a simple and efficient probe for aromaticity [17]. NICS is the computationally calculated value of the negative magnetic shielding at some selected point in space of the molecule, generally, at a ring or cage center. Aromaticity is denoted by negative NICS data (–11.5 for benzene, –11.4 for naphthalene) whereas positive values of NICS denote antiaromaticity (28.8 for cyclobutadiene). In addition, nonaromatic systems possess small NICS values (–3.1 for 1,3-cyclopentadiene). NICS is proven to be a convenient indicator of aromaticity that often correlates very well with the other energetic, structural and magnetic criteria [18–21]. Overall of a polycycle can be represented by resonance energies and magnetic susceptibilities, however they do not provide information about the individual rings. Fortunately, local aromaticity of individual rings of polycyclic compounds are judged by computing NICS, which makes it be an effective probe for aromaticity.

Another index for aromaticity, which is geometry-based, is named as Harmonic oscillator measure of aromaticity (HOMA) [14]. HOMA is different from the other geometry-based indices in terms of consideration of a reference bond length or bond order. In HOMA model an idea of the optimal bond length is taken as a reference instead of the mean bond. HOMA data are between 0 and 1. A non-aromatic system gets 0 HOMA value, on the other hand, 1 is obtained for a system where full  $\pi$ -electron delocalization occurs (benzene). The extent of  $\pi$ -electron delocalization (aromatic character) of six membered heterocycles can be quantified by HOMA.

The following formula can be used to calculate HOMA:

HOMA = 
$$1 - \frac{\alpha}{n} \sum (R_{\text{opt}} - R_i)^2$$
 (1.1)

$$= 1 - \frac{\left[\alpha_{\rm CC} \sum \left[R_{\rm (CC)opt} - R_{\rm i}\right]^2 + \alpha_{\rm CX} \sum \left[R_{\rm CXopt} - R_{\rm i}\right]^2\right]}{n}$$
(1.2)

In this equation, a is the normalization constant and n is the number of chemical bonds considered. The optimum bond length is represented by  $R_{opt}$  that is obtained when full delocalization of  $\pi$ -electrons, and  $R_i$  are the computed bond lengths. For CC bonds a is fixed to 257.7 which gives HOMA = 0 for a non-aromatic system (e.g. Kekule´ structure of benzene), and HOMA = 1 is found for an aromatic compound whose all the bonds are computed to be equal to the optimal bond length value.

For CC bonds,  $R_{opt}$  is assumed to be equal to 1.388 Å when the compound is realized as a full aromatic system. PDI, ATI and FLU indices [22] and HOMA index [23–25] have been studied in the literature to decide the relationship between substituent effect and the aromatic nature of aza analogs of naphthalenes, recently.

In this chapter, the aromaticity of mono, di, tri and tetraazaphenanthrene derivatives was computed by the application of Density Functional Theory using the B3LYP hybrid functional and 6-31G+(d,p) basis set. Introduction of an heteroatom, nitrogen in the present case, creates azaphenanthrenes. By means of centric perturbation of one, two, three and four nitrogens at different positions, mono, di, tri and tetraazaphenanthrene derivatives are structurally obtained from phenanthrene, respectively. It is obvious that the introduction of nitrogens will reduce the aromaticity of the parent phenanthrene structure due to less effective electron localization because of the disturbed ring current arising from electronegativity of the nitrogens at the perturbation site. The goal of the present research article was to study the substituent effect on the aromaticity of azaphenanthrenes by means of NICS and HOMA indices. The effect of the position of NO<sub>2</sub> substituent on the present systems has been theoretically studied by the application of density functional theory (DFT) calculations focusing especially on NICS data. Moreover, HOMA indices have been calculated by the formula for all the compounds to judge the aromaticities. Lastly, a comparison has been done with NICS and HOMA data to gain inside whether magnetic or geometry-based criteria better defines the aromatic characters.

## 1.2 Method of calculation

Semi-empirical PM3 self-consistent field molecular orbital (SCF MO) method has been applied for initial geometry optimizations for all the structures leading to energy minima [26, 27] at the restricted level [28]. Afterwards, geometry optimizations were performed within the framework of density functional theory (DFT, B3LYP) [29, 30] at the level of 6-31G(d,p) (restricted closed-shell) [27]. B3LYP is an exchange term consisting of hybrid Hartree–Fock and local spin density (LSD) functions with Becke's gradient correlation to LSD exchange [31]. Vosko, Wilk, Nusair (VWN3) local correlation functional [32] and Lee, Yang, Parr (LYP) correlation correction functional [33] construct the correlation term of B3LYP. SCF-HF results are improved by the B3LYP method whose predictions are in qualitative agreement with experimental data [34–36].

The normal mode analysis performed for all the structures. Each structure does not yield any imaginary frequencies for the 3N-6 vibrational degrees of freedom, where N is the number of atoms in the system, which indicates that the geometry of each molecule represents a local minimum on the potential energy surface. NMR shielding data [37] were computed using the Gauge-Independent Atomic Orbital method [38] with the restricted closed shell method performing 6-31 + G(d,p) basis set over B3LYP/6-31G(d,p) optimized geometries. NICS values were calculated theoretically by obtaining NMR shielding at the ring centers, NICS(0). Gaussian 09 W package program was used for the geometry optimizations and NICS calculations of the present systems [39].

## **1.3 Results and discussion**

Substituted phenazine cores are usually found in natural products, dyestuffs, pesticides, and antibiotics, which makes them important biologically active motifs. A majority of them are produced naturally by bacteria from diverse genera including Pseudomonas, Pelagiobacter, Vibrio and Streptomyces species [40].

Both theoretical and experimental studies on the effect of centric substitution of an heteroatom to the parent ring, and/or substitution of an heteroatom or heterogroup with the outer hydrogens of aromatic molecules have always found application in the literature. In the present article, mono, di, tri and tetraazaphenanthrene derivatives and their substituted (**NO**<sub>2</sub>) counterparts have been investigated theoretically by the application of B3LYP/6-31 + G(d,p) level of theory in order to decide their stabilities and aromaticities.

The mono and/or dicentric perturbation on positions of ring fusions are not taken into account since non-aromatic systems are resulted in those cases. The molecules were named according to the positions of the nitrogens on the system from **Ph\_1** to **Ph\_1\_2\_3\_4** for tetraazaphenanthrene (see Figure 1.3). **Ph** represent phenanthrene and the numbers indicate the position of the heteroatom substitution.

## **1.4 Energetics**

The aforementioned method has been used to obtain the zero point corrected total electronic energies of the present compounds. The total energies (in a.u.) and corresponding relative energies (in kJ/mol) of the systems are given in Table 1.1. The



**Figure 1.3:** Chemical structures of mono, di, tri and tetraazaphenanthrene derivatives. The numbering in **Ph** indicates the positions of aza substitutions.

Structure	Total Energy	Relative Energy
Ph	-539.53865526	
Ph_1	-555.58020638	0
Ph_2	-555.57523782	12.55
Ph_3	-555.57589079	10.90
Ph_4	-555.57711401	7.81
Ph_5	-555.57775942	6.18
Ph_1_2	-571.58245993	95.11
Ph_1_3	-571.62011790	0
Ph_1_4	-571.61467372	13.75
Ph_1_5	-571.61356400	16.55
Ph_2_3	-571.61686438	8.22
Ph_2_4	-571.61873150	3.50
Ph_2_5	-571.61353711	16.62
Ph_3_4	-571.61347597	16.77
Ph_3_10	-571.61314591	17.61
Ph_1_2_3	-587.60516311	64.76
Ph_1_3_4	-587.63080594	0
Ph_1_2_3_4	-603.60077732	

Table 1.1: Total energies (a.u.) and corresponding relative energies (kJ/mol) of the two series.