CHAPTER 4

Multifunctional magnetic materials of organic origin for biomedical applications: A theoretical study

Abstract

In fourth chapter six different diradical systems based on azulene coupler and nitronyl nitroxide radical moieties are studied theoretically. Among them, three ferromagnetic diradicals are chosen for further calculation to assess their usability in different biological applications such as two-photon absorption photodynamic therapy (TPA-PDT) and magnetic resonance imaging contrast agents (MRICA). The TPA cross-section values are calculated to judge their efficiency as TPA-PDT photosensitizing agents. Calculated values of TPA cross-section lie in the range of commonly used photosensitizers for PDT. It is seen that the ferromagnetic diradicals can act as very good MRI contrast agents due to their high magnetic anisotropy characteristics. In connection to the magnetic anisotropy, the zero-field splitting (ZFS) parameters are also computed using density functional theory (DFT) based methods. It is found that the proposed diradicals can show good relaxation behaviour and consequently act as efficient MRI contrast agents. Thus, one can anticipate the multifunctional biological activity of these diradicals.

4.1. Introduction

In the past few years, organic magnetic materials have attracted the attention of the materials science community due to its interesting electrical, magnetic and nonlinear optical (NLO) properties. Appealing magnetic behaviour in reduced dimensions, diverse functional characteristics such as photosensitivity, fluorescence activity, highly efficient NLO property etc. promote their potential applications in photonic devices *viz.,* optical switching, three dimensional memory storage and photodynamic therapy (PDT).[156, 157] PDT is recognized as a highly effective treatment to fight oncological diseases in recent times.[158, 159] PDT requires a photosensitizer, which transfers its triplet state energy to molecular oxygen when activated by light. This leads to the genesis of reactive singlet oxygen species ($^1O_2$) capable of causing oxidative damage to biological substrates and ultimately lead to selective and irreversible apoptosis of malignant tissues, without causing damage to the adjacent healthy ones.[160, 161] The excitation of photosensitizers, induced by two-photon absorption (TPA), is considered as a promising strategy in PDT and this is popularly known as two-photon photodynamic therapy (TP-PDT).[157, 162] Two-photon absorption is a third-order nonlinear optical process in which excitation occurs by the simultaneous absorption of two photons at longer wavelengths instead of a single-photon excitation at a shorter wavelength.[163] A great deal of attention is paid to TPA property of organic π-conjugated systems because of their large nonlinear optical response.[164, 165] In particular the design, preparation and application of efficient multifunctional organic diradicals are of enormous importance in the field of biomedical research.[166, 167] The existence of both magnetic and optical properties in the same molecule will certainly make them appropriate candidates in the field of biophotonics.[168, 169]

The increase in interest towards nitronyl nitroxide (NN)[170, 171] stems not only from their use as building blocks in the design of molecular magnetic materials,[172] such as purely organic ferromagnetic ordered solids,[173, 174] metal organic exchange coupled complexes[175-177] but also as new agents in bio imaging.[178-180] NN radical is known to be exceptionally stable, easy to prepare and able to generate co-operative magnetic properties.[181] Moreover it has been established that the nitronyl nitroxide radical shows cell permeability, biocompatibility and *in vivo* stability of the nitroxide-drug bonds.[182, 183] Although a number of NN based diradicals have been synthesized and experimentally investigated,[184] combined electro-optic and magnetic materials based on NN diradicals have not received adequate attention. A number of previous reports reveal that the couplers between two radical centers play a decisive role for the magnetic characterization of the

systems.[185, 186] Generally, magnetic coupling arises from spin polarization and spin delocalization.[187] Nevertheless, the magnetic interaction between two radical centers normally depends upon the nature and the spatial linkage to the coupler. Thus by a judicious choice of the coupler and by modifying the spatial orientation of the coupler, the magnetic interaction may change in a useful manner so that the magnetic molecule have some multifunctional features.[187-189] In a nutshell, choice of coupler will be the key factor for designing efficient multifunctional materials.

Highly aromatic couplers are known to induce strong magnetic interaction in organic diradicals.[190] The high aromaticity of azulenes and their strong tendency to retain aromaticity upon exposure to magnetic interaction[191] make them suitable as coupler between radical centers. Though aromaticity of azulene compared to one of its isomer naphthalene is less, it has long been considered to be an interesting candidate for the application in optoelectronic materials due to its unique electronic and optical properties such as large permanent dipole moment, intense blue colour and the domination of fluorescence from $S_2 - S_0$ with low emission intensity.[192, 193] Stimuli responsive behavior and high luminescence intensity of azulene derivatives also became recognized in recent research.[194, 195] Despite quite a large number of theoretical calculations on the influence of the functional bis-substitution pattern of azulenes on their electronic properties, the theoretical investigation of magnetic and nonlinear optical properties of various diradical substituted azulene derivatives is lacking. Thus there is certainly a possibility of developing multifunctional ferromagnetic molecules with azulene as a coupler and nitronyl nitrixide as radical centers.

In this work six diradicals based on suitable substitution of NN radical in different positions of azulene coupler (Scheme 4.1) are considered as the reference systems of the present theoretical study. The estimation of magnetic exchange coupling constant values (J) for all of these diradicals has been performed in the gas phase. The process of calculation is straightforward and well-established in the case of gas phase. However, for calculation in water and in *blood plasma* medium, the polarized continuum model (PCM) has been adopted. TPA cross section (σ) has been calculated to assess the efficiency of the proposed radicals for multifunctional uses. In the literature it has been shown that diradicals of organic origin can be effective and less hazardous for use in magnetic resonance imaging (MRI) as contrast agents.[196, 197] In order to achieve a good MRI contrast activity, large longitudinal relaxation rate of the contrast agents is highly desired. Zero-field splitting (ZFS) magnitude is the key parameter to ascertain the longitudinal relaxation rate (*vide infra*) and the suitability of a diradical as MRI

contrast agents (MRICAs).[198] Hence, we have evaluated the axial and rhombic ZFS parameters (*D* and *E*) of the diradicals so to assess their aptness as MRICAs.
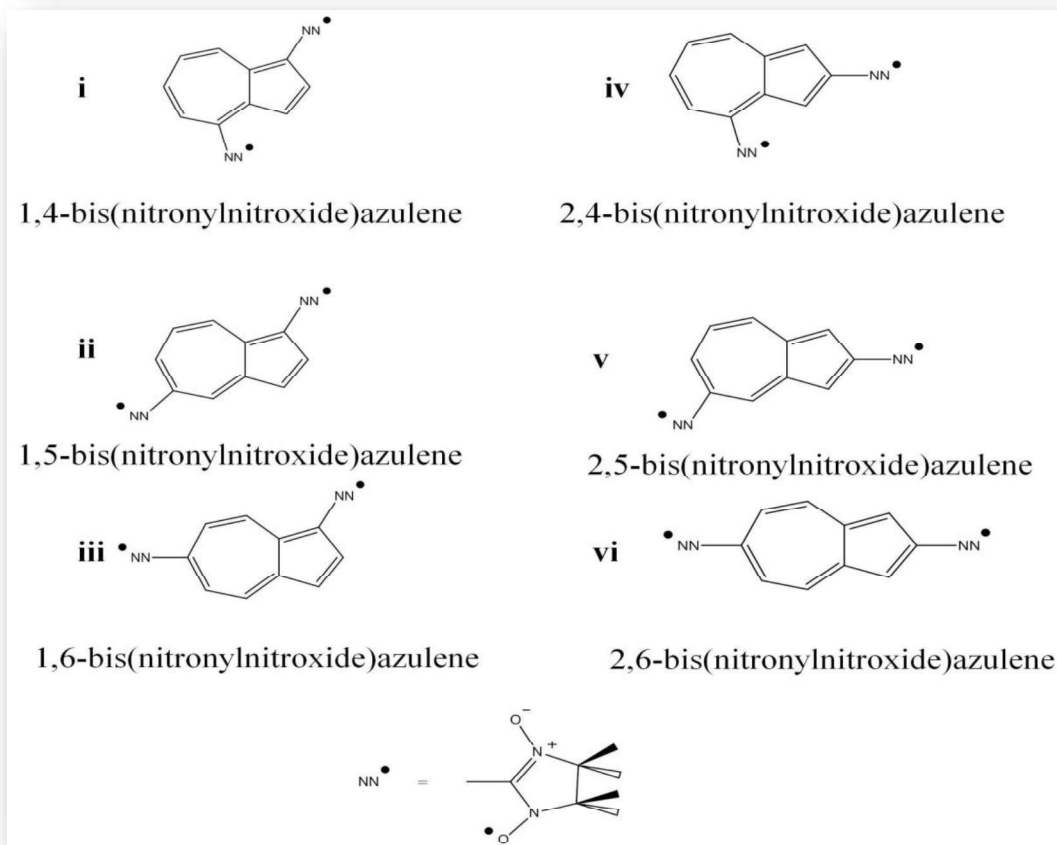
Scheme 4.1. Schematic representation of the diradicals under investigation.

4.2. Theoretical Background

The magnetic exchange interaction between two magnetic sites 1 and 2, is in general expressed by the Heisenberg spin Hamiltonian,

$$\hat{H} = -2J\hat{S}_1\hat{S}_2 \tag{4.1}$$

where S_1 and S_2 are the spin angular momentum operators of spin-sites 1 and 2 respectively, and J is the exchange coupling constant. A positive J-value indicates a ferromagnetic interaction, whereas a negative value of J signifies an antiferromagnetic interaction. To evaluate the exchange coupling constant with reasonably less computational effort, Noodleman[199, 200] has proposed an unrestricted spin polarized broken symmetry (BS) formalism in the DFT framework. The BS state is not a pure spin state, but a state of mixed spin

symmetry with lower spatial symmetry. Depending on the extent of the magnetic interaction between two magnetic sites, many scientists have developed different formulae to estimate J using the BS approach.[201-204] Ideally, for diradicals the computed average $\langle S^2 \rangle$ values for triplet and BS states should be exactly 2.00 or 1.00 respectively. However in reality, their difference is not exactly unity, showing a clear indication of the spin contamination problem. In order to neutralize the spin contamination error associated with the BS state, one can use a spin projection technique. For estimating the J-values of diradicals of organic origin, the following expression by Yamaguchi et al.[201, 205, 206] is the most widely applied[186, 207, 208] and has been used by us in this work

$$J_Y^{DFT} = \frac{(E_{BS}^{DFT} - E_{HS}^{DFT})}{\langle S^2 \rangle_{HS} - \langle S^2 \rangle_{BS}}$$ (4.2)

where E_{BS}, $\langle S^2 \rangle_{BS}$, and E_{HS}, $\langle S^2 \rangle_{HS}$ are the energy and average spin square values for the corresponding BS and high spin (HS) states, respectively. All the above mentioned calculations are implemented through the Gaussian 09W quantum chemical package.[142]

The electron spin correlation time is important for clear MRI scans with enhanced contrast. The ZFS helps to get an estimation of the electron spin correlation time,[209] and is also one of the important parameters to characterize the geometric and electronic properties of a radical with S > 1/2.[210] The zero field splitting is treated in the second order of the perturbation theory where two interactions are taken into account, namely the direct spin–spin (SS) interaction and (second-order) spin-orbit coupling (SOC),[210] however, the SS coupling contribution is the main source of ZFS in the case of organic radicals which are formed with light elements.[211] The ZFS value arising from the SS interactions can be estimated through an effective spin Hamiltonian

$$\hat{H}_{ZFS} = \sum_{\mu,\nu} D_{\mu\nu} \hat{S}_\mu \hat{S}_\nu$$ (4.3)

where $D_{\mu\nu}$ are the components of the ZFS tensor, $\hat{S}_\mu$ is the μth Cartesian component of the total electron–spin operator. After diagonalization and subsequent reframing of the molecular coordinate, Equation (4.3) optimizes to

$$\hat{H}_{ZFS} = D\left(\hat{S}_Z^2 - \frac{1}{3}\hat{S}^2 \right) + E(\hat{S}_X^2 - \hat{S}_Y^2)$$ (4.4)

where D and E are axial and rhombic ZFS parameters respectively.[212] The spin–spin coupling interaction appears as a dipole-dipole interaction,[213]

$$\hat{H}_{SS} = \frac{\alpha^2}{2} \sum_{ij} \left[\frac{\vec{s}_i \cdot \vec{s}_j}{r_{ij}^3} - \frac{3(\vec{s}_i \cdot \vec{r}_{ij})(\vec{s}_j \cdot \vec{r}_{ij})}{r_{ij}^5} \right] \tag{4.5}$$

The ground state Kohn-Sham determinant approximates the ZFS tensor components as expectations over the single determinant,[214]

$$D_{\mu\nu}^{(SS)} = \frac{g_e}{4} \frac{\alpha^2}{S(2S-1)} \langle OSM_S | \sum_I \sum_{J \neq I} \frac{r_{ij}^2 \delta_{\mu\nu} - 3(r_{ij})_\mu (r_{ij})_\nu}{r_{ij}^5} \times \left\{ 2\hat{S}_{iz}\hat{S}_{jz} - \hat{S}_{ix}\hat{S}_{jx} - \hat{S}_{iy}\hat{S}_{jy} \right\} | OSM_S \rangle. \tag{4.6}$$

In the above, α is the fine structure constant, g_e is the gyromagnetic ratio. The operators $\hat{S}_{i\mu}$ signify the μ'th components of i'th spin vector, and r_{ij} is the distance between spin sites i and j, while μ and ν run over x, y, z coordinates. McWeeny and Mizuno expressed the above equation using the spin density matrix as[215]

$$D_{kl}^{(SS)} = \frac{g_e}{4} \frac{\alpha^2}{S(2S-1)} \sum_{\mu\nu} \sum_{\kappa\lambda} \left\{ P_{\mu\nu}^{\alpha-\beta} P_{\kappa\lambda}^{\alpha-\beta} - P_{\mu\kappa}^{\alpha-\beta} P_{\nu\lambda}^{\alpha-\beta} \right\} \times \langle \mu\nu | r_{12}^{-5} \left\{ 3r_{12,k} r_{12,l} \right\} \left(-\delta_{kl} r_{12}^2 \right) | \kappa\lambda \rangle \tag{4.7}$$

Here, $P^{\alpha-\beta} = P^\alpha - P^\beta$ is the spin density matrix in the atomic orbital basis, and now $\mu, \nu, \kappa, \lambda$ label the basis orbitals.[211] The ZFS parameters D and E are determined from the tensor components $D_{kl}^{(SS)}$, as[216]

$$D = D_{ZZ} - \frac{1}{2}(D_{XX} + D_{YY}) \tag{4.8}$$

$$E = \frac{1}{2}(D_{XX} - D_{YY}) \tag{4.9}$$

and in turn determine the static ZFS magnitude (a_2) through

$$a_2 = \sqrt{\left(\frac{2}{3} D^2 + 2E^2 \right)} \tag{4.10}$$

From this a_2, the longitudinal electron–spin relaxation rate $\frac{1}{T_{1e}}$ can be estimated by,[217]

$$\frac{1}{T_{1e}(B_0)} = \frac{2}{5} a_2^2 \tau_R \left[\frac{1}{1 + \omega_0^2 \tau_2^2} + \frac{4}{1 + 4\omega_0^2 \tau_2^2} \right] + \frac{12}{5} a_{2T}^2 \tau' \left[\frac{1}{1 + \omega_0^2 \tau'^2} + \frac{4}{1 + 4\omega_0^2 \tau'^2} \right] \tag{4.11}$$

Where B_0 is the external magnetic field, ω_0 is the Larmor frequency, τ_2 and τ' are the reduced spectral densities and a_{2T} is the transient ZFS magnitude. Larger a_2 values correspond to a faster relaxation rate $1/T_{1e}$.[217]

Despite the well established formal theoretical description of TPA,[218] the theory has only been applied in the context of physics of atoms and small molecules. The two-photon-absorption cross section is related to the imaginary part of the third-order polarizability as[87, 219, 220]

$$\sigma_{TPA}(\omega) = \frac{4\pi^2 \hbar \omega^2}{n^2 c^2} L^4 \operatorname{Im}\langle \gamma(\omega, \omega, -\omega)\rangle \qquad (4.12)$$

where $\hbar$ is Plank's constant, c is the speed of light, n is the refractive index of the media, L is the local field factor. $\langle \gamma \rangle$ is the second hyperpolarizability, average over all orientations, which is represented as

$$\langle \gamma \rangle = \frac{1}{15}\left[3\sum_i \gamma_{iiii} + \sum_{i \neq j}\left(\gamma_{iijj} + \gamma_{ijji} + \gamma_{ijij}\right)\right] \qquad (4.13)$$

where indices i and j refer to spatial directions x, y, and z.[221] The evaluation of the third-order polarizability is done by the perturbative sum-over-state (SOS) method utilizing the ground- and excited-state energies, state dipoles, and transition dipole values.[222, 223]

4.3. Computational Details

The gas phase molecular geometry of all the azulene diradicals have been fully optimized with the unrestricted B3LYP functional using the 6-311g(d,p) basis set in Gaussian 09W suite of program.[142] The magnetic exchange coupling constant (J) is estimated from the single point energies of the triplet and BS state at the UB3LYP/6-311++g (2df, 2p) level utilizing Equation (2). The ZFS parameters (D and E) have been calculated using BPW91 functional, EPR-II basis set in ORCA suit of software.[224] EPR-II basis set has long been considered to be useful for calculating the D values in case of organic diradicals.[225] The validity of this methodology for computing D and E is tested by comparing the computed value of D and E against the experimental value available for a diradical synthesized by Rajca. The experimental ZFS parameter has been reported as -1.22×10^{-2} cm^{-1}, which is in close agreement with the computed D value (-1.60×10^{-2} cm^{-1}). For this correlation of our computed results with the experimentally reported data by Rajca *et al.*, the same combination of basis set and functional is used for the

estimation of the *D* parameters for the systems under investigation. In order to check the effect of solvent on calculated properties, the *J* and *D* values are also calculated within polarizable continuum model (PCM) using the dielectric constants of water and *blood plasma* (80 and 58 respectively), which are the most common solvents in human body.

The computation of TPA cross section values have been carried out at UB3LYP/6-311++g (2df, 2p) level of theory in DALTON software.[226]

4.3. Results and discussions

The optimized geome4tries of the designed diradicals are shown in Figure 4.1. Frequency calculation on the optimized geometries showed no imaginary frequency for any of the molecules, which indicate intrinsic stability of the optimized structures (zero point energy corrected values are also given in the supporting information in Table S2). The gas phase magnetic exchange coupling constant (*J*) values are presented in Table 4.1. Systems **i, iii** and **v** are found to be ferromagnetic and the systems **ii**, **iv** and **vi** are antiferromagnetically coupled. The ferro- and antiferro-magnetic behaviour of the azulene coupled diradical systems can be justified through the popular spin density alternation rules.[227, 228] The spin-density alternation can also be visualized through the spin density plots presented in Figure 4.2., where one can clearly see that the radicals coupled through an odd and even number of conjugated atomic centers always lead to ferro- and antiferromagnetic interactions respectively. A close inspection of Figure 2 further reveals an interesting feature of the spin density alternation. The carbon atoms situated at the junction of two fused five and seven membered rings in azulene always carry similar spins despite being neighbours. It appears that the two junction-carbon atoms in **i, iii** and **v** behave as single units in spin density alternation protocol. Owing to their biomedical relevance we consider only the ferromagnetic systems, *i.e.,* **i, iii** and **v** for further calculations
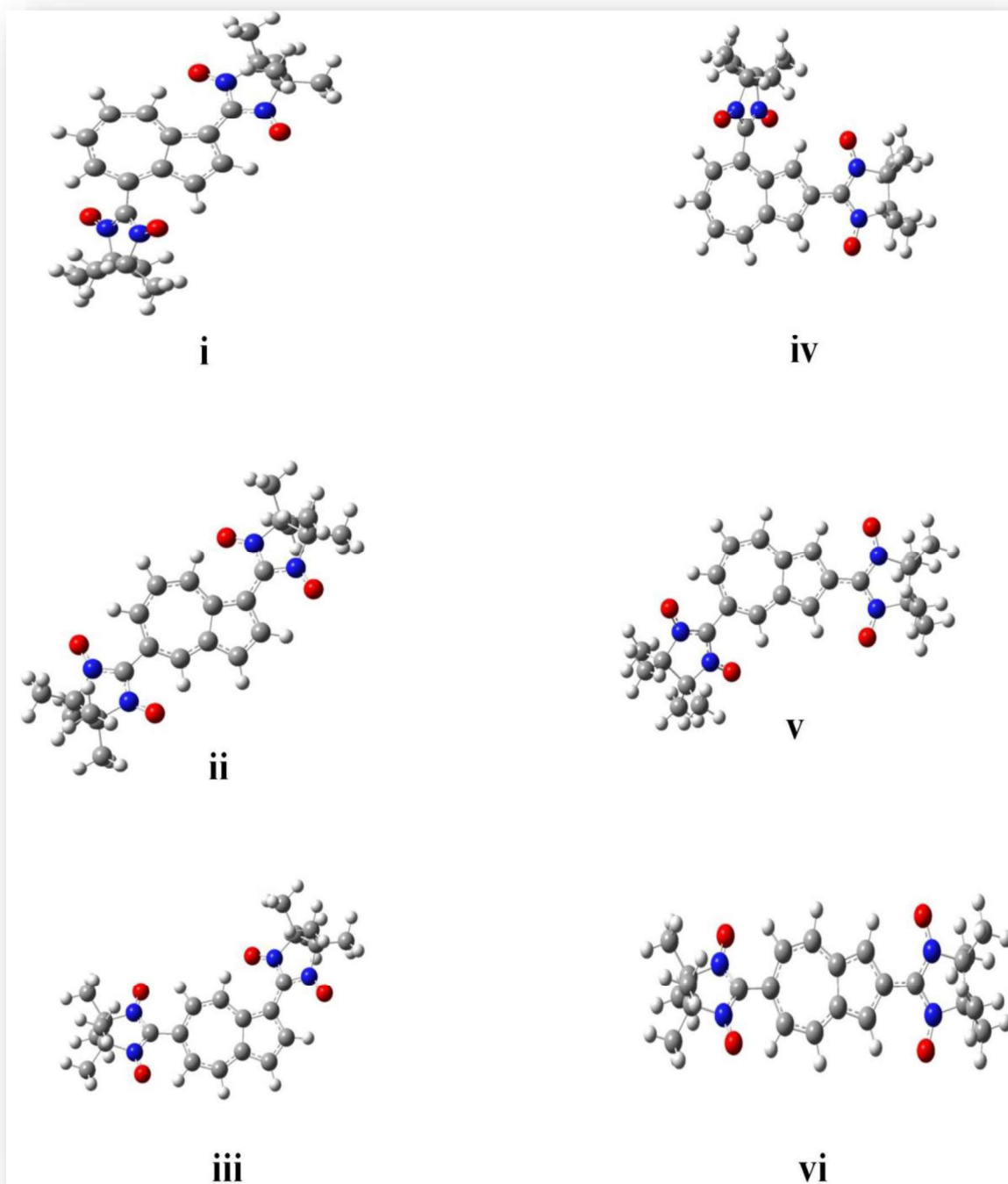
Figure 4.1. Optimized molecular geometry of the diradicals obtained through unrestricted B3LYP exchange correlation functional using the 6-311g (d,p) basis set.

Table 4.1. *Calculated absolute energies in atomic units (au),* $\langle S^2 \rangle$ *values, intramolecular magnetic exchange coupling constants (J in cm^{-1}) between two radical centers for the designed diradicals at UB3LYP/6-311++g (2df, 2p) level.*

| Diradicals		Energy (au)	$\langle S^2 \rangle$	J in cm^{-1}
i	Triplet	−1452.7267132	2.115519	12.75
	BS	−1452.726656	1.130897	
ii	Triplet	−1452.7346583	2.096137	−193.22
	BS	−1452.7355085	1.130392	
iii	Triplet	−1452.7330113	2.131788	47.70
	BS	−1452.7327901	1.114097	
iv	Triplet	−1452.7333679	2.106828	−81.77
	BS	−1452.7337341	1.123951	
v	Triplet	−1452.7411477	2.149931	90.37
	BS	−1452.7407227	1.117795	
vi	Triplet	−1452.7381936	2.108376	-228.89
	BS	−1452.7391866	1.156251	
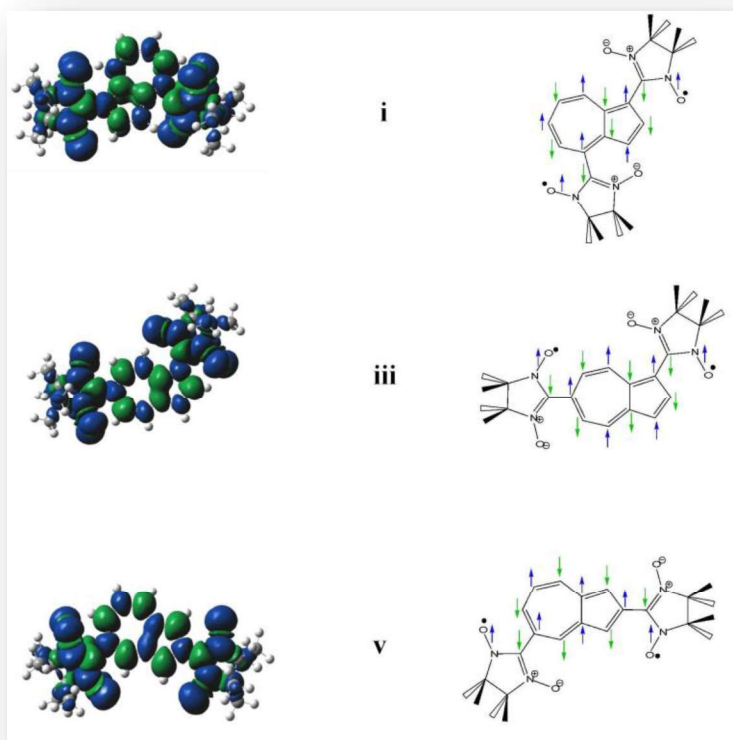
Figure 4.2. *Spin density plots of ferromagnetic azulene diradicals. Green and blue surfaces indicate up and down spin density. Same color code is used for schematic representation of spin alternation, i.e., blue and green arrow for up and down spin respectively.*

Extensive study of two-photon photodynamic therapy revealed that the treatment is relatively benign and gives finer cosmetic outcomes compared to other PDT techniques. In those methods excitation of the drugs are performed through visible light which has very low penetrability into human tissues.[229, 230] Simultaneous absorption of two near-IR photons is much more penetrating through tissues compared to visible light photons. Hence, excitation of the photosensitizer through near-IR photons is more desirable to destroy cancer cells present in deeper tissues.[231, 232] Two-photon PDT also ensures greater penetration depths and highly-selective targeting through intense laser pulse processes. TPA cross-section (σ_{TPA}) estimates the efficacy of a photosensitizer that undergoes two-photon absorption. It is measured in Göppert-Mayer units (1 GM = 10^{-50} cm^4 s photon^{-1} molecule^{-1}). The TPA cross-sections of existing photosensitizers are in the order of 1–100 GM.[233] In a recent report Zhao *et al.*[234] studied the spectroscopic properties of Chlorophyll derivative photosensitizer (CDP) and their TPA cross section is measured as 31.5 GM. The results of the two photon photodynamic therapy (TPPDT) test showed that CDP can kill all of the tested cancer cells. Hence, suitable design of compounds with higher TPA cross-sections is always desirable to ensure efficient phototherapeutic applications. Generation of singlet oxygen ($^1\Delta_g$) is the key to phototherapeutic activity of the photosensitizers in PDT. A good singlet oxygen yield (Φ_Δ) is desired for photo-biological cell damage or apoptosis. It has been seen that the insertion of radical moieties in a photosensitizer greatly enhances Φ_Δ.[235] Thus a diradical system will be the best candidate for use as photosensitizer in photodynamic therapy. In the present study we have calculated σ_{TPA} of the designed diradicals which are reported in Table 4.2. It is found that the TPA cross-section values lie in the reported range of the presently used photosensitizers. Among the three designed ferromagnetic diradicals, **v** shows the highest σ_{TPA} value of 21.1 GM.

Although very promising as noninvasive and safe protocols of cancer treatment, PDT is challenging in connection with the delivery of the photosensitizer to the infected tissue.[51] To ensure the monomeric distribution of the photosensitizing agent, diagnostic imaging techniques are preferred compared to regular drug delivery methods.[236] Magnetic resonance imaging has emerged as a powerful imaging technique in recent years. MRI, with the use of contrast agents can provide highly sensitive imaging with minute three dimensional topographical details *in vivo*. Hence, if one can integrate contrast-enhanced MRI imaging capability with PDT, the resulting imaging guided PDT can prove to be the most appreciable strategy for cancer treatment. The design of materials with good imaging and photosensitizing capability is therefore the requirement for developing improved multifunctional agents.

Table 4.2. *The spin-spin ZFS parameter D_{Total} (cm^{-1}), static ZFS magnitude a_2 (cm^{-1}), rhombic ZFS parameter (E) for each ferromagnetic diradical at BPW91/EPR-II and two photon absorption cross section (σ_{TPA} in GM), for the same diradicals at UB3LYP/6-311++g(d,p) level.*

Diradicals	σ_{TPA} (GM)	D_{Total} (cm^{-1})	E (cm^{-1})	a_2 (cm^{-1})
i	3.8	-10.03×10^{-2}	-1.7×10^{-2}	8.5×10^{-2}
iii	5.0	-11.6×10^{-2}	-1.51×10^{-2}	9.7×10^{-2}
v	21.1	-10.6×10^{-2}	-0.74×10^{-2}	8.7×10^{-2}

A site-specific MRI contrast agent with a high rate of relaxation of water protons in the target cell is central to efficient magnetic resonance imaging. It is quite evident from the discussion in the previous section and Equation (11) that the ZFS magnitude (a_2) is directly proportional to the longitudinal relaxation rate ($1/T_{1e}$). With the increase in the value of $1/T_{1e}$, the observed MRI signal is enhanced. In the present work, the ZFS parameter D and static ZFS magnitude (a_2) of the three ferromagnetic systems, namely, **i**, **iii** and **v**, have been estimated and is reported in Table 2. It is notable from Table 2 that all the ferromagnetic diradicals possess high value of D in the range of -8.5×10^{-2} cm^{-1} to -9.7×10^{-2} cm^{-1}. Rajca et al. in one of their pioneering works reported nitroxide based diradicals, synthesized and already been established as a MRICA of organic origin, to have D values in the range of -1.2×10^{-2} to -1.7×10^{-2} cm^{-1}.[196, 197] A diarylnitroxide triplet diradical with D and a_2 values of -1.223×10^{-2} and 1.02×10^{-2} cm^{-1} respectively is also found to be usable as MRICA.[198]

In order to gain an assurance of the *in vivo* functionality of the designed systems, we have calculated the magnetic exchange coupling constant (J) and the zero field splitting parameters (D) in water and as well as in blood plasma medium and the results are reported in Table 4.3. It is clear that the variations in J and D values of all the designed systems in different media are negligible.

Table 4.3. *The magnetic exchange coupling constants (J) and ZFS parameter (D) values for the proposed ferromagnetic diradical systems in gas phase, water and blood plasma media, computed using PCM model using UB3LYP/6-311++g(2df,2p) and BPW91/EPR-II method.*

Diradicals	J (cm^{-1})			D (cm^{-1})		
	Gas Medium	Water Medium	Blood Plasma	Gas Medium	Water Medium	Blood Plasma
i	12.75	12.40	12.42	-10.03×10^{-2}	-10.3×10^{-2}	-10.6×10^{-2}
iii	47.70	41.68	43.03	-11.6×10^{-2}	-10.6×10^{-2}	-10.6×10^{-2}
V	90.37	81.59	81.64	-10.6×10^{-2}	-10.9×10^{-2}	-10.9×10^{-2}

4.4. Conclusion

In the present computational study we have considered the magnetic and optical properties of a few azulene based diradical systems. We have studied six diradical systems based on nitronyl nitroxide radical moiety and azulene as coupler. The magnetic property has been assessed through the magnetic exchange coupling and magnetic anisotropy. The calculated magnetic exchange coupling parameters J depict that among the six diradicals three are ferromagnetic, and three are antiferromagnetic. The magnetic exchange coupling constants have been corroborated through spin density alternation protocol. The spin density analyses of the three ferromagnetic diradicals depict an interesting alternation behavior in the azulene coupler. The junction carbon atoms of the two rings in azulene coupler always show similar spin density despite being neighbors. This behavior is a fascinating variation of the spin density alternation rule. The ability of the ferromagnetic diradicals as photosensitizer in photodynamic therapy is evaluated through the computation of the two-photon absorption cross-section. The integrative photodynamic therapy (IPDT) of tumors relies on the combined use of different factors that enhance the usefulness of IPDT.[237] The observed TPA cross-section values range in the reported limit of commonly used photosensitizing agents. Another dimension of the multi-property diradical system has also been explored in this work. The magnetic anisotropy of the ferromagnetic diradicals has been estimated through the zero-field splitting parameter D. A negative ZFS parameter suggests the tendency of the spin vector to orient along a specific Cartesian direction. All the three ferromagnetic diradicals show negative D values. Radical systems with negative ZFS parameters have been proved to be usable as MRI contrast agents.[188] It has long been shown that the larger the ZFS magnitude a_2, larger is the spin relaxation time

and the better an MRICA is.[198] The ZFS magnitude a_2 is directly proportional to the ZFS parameter D. In the designed ferromagnetic diradicals, the ZFS parameters are found to be significantly high as for organic radical systems. The values are at least one order of magnitude higher compared to reported diradical systems usable as MRICA. Ferromagnetic systems are used as efficient probe in the magnetic hyperthermia, a popular treatment in oncology. These diradicals can also be sought for a lateral use as MRICA in magnetic resonance imaging, which is very often utilized for the detection of cancer. Treatment of interstitial tumors with PDT demands the delivery of photosensitizers to the precise location of tumor tissues for effective light irradiations. Thus a single agent that can be injected to the infected body to image tumors through MRI and simultaneously treat them by exposing to light through PDT is greatly welcomed as a proficient cancer treatment protocol. In summary we propose that if synthesized these diradical systems can promote the "see and treat" method[238] by proving themselves efficient in multifarious therapeutic function such as magnetic hyperthermia, MRI contrast agents and photodynamic therapy applications.