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# An ionic receptor for Zn<sup>2+</sup> metal ion using synthesised bis-formylpyrazole calix[4] arene and its computational study

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#### ABSTRACT

Newly synthesised receptor Bis-(1,3-diphenyl-pyrazolyl methylene acetohydrazide)Calix[4]arene (DPPMACA) was evaluated for cation binding ability. The receptor DPPMACA selectively interact with  $Zn^{2+}$  metal ion as assessed through UV-visible spectroscopy with a bathochromic shift of 14 nm but gave negligible response for other metal cations used as their sulfates. The stoichiometry observed as 1:1 with stability constant  $6.438 \times 10^3 M^{-1}$ . Additionally, computational visions were concentrated for studying the stability and spectroscopic analysis of the DPPMACA- $Zn^{2+}$  complex using docking, molecular dynamics simulations and density functional theory (DFT) along with time-dependent density functional theory (TD-DFT). The calculations significantly supplement the findings and elucidate the structural geometry and mode of interactions in supramolecular complexation. Herein, we witnessed that DPPMACA was selectively stabilized by Metal-donor and Metal-acceptor contacts with  $Zn^{2+}$  to generate a low-energy complex. These findings are of wide interest, especially because  $Zn^{2+}$  is a well-known biological important cation.

#### ARTICLE HISTORY

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**KEYWORDS** Formylpyrazole; calixarene; UV-vis; Zn<sup>2+</sup> sensor; DFT calculation



#### 1. Introduction

The development of molecular receptors is very agile research area as it provides substantial binding sites for multiple ions (1-6). Calixarenes provide framework as host molecules due to presence of cavity, functionalization sites and efforts are continuously made to design

molecular receptors for recognition systems capable of sensing charged or neutral molecules (7–9). These receptors reinforce theories on weak intermolecular interactions for sensing, separation, catalysis and for many other applications of supramolecular technology (1–7). Mostly metals of d block shows interactions with receptors and plays vital

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role in functioning of a vast number of widely differing bio-systems. When these metals are present in excess to biological processes they cause excessive damage. Acute poisoning occurs due to ingestion of copper, cadmium and zinc salts. Further accumulation results in toxicity to liver, kidneys, brain, lungs, heart and central nervous system (10–12).

Macrocyclic receptors are efficient for coordination with alkali and alkaline earth metals. But the derivatives of macrocyclic molecules (calix(aza-)crowns) are also able to interact with softer di- and trivalent cations. The schiff-base of calix[4]arenes are also investigated to form complex with heavy transition metals and lanthanides. Calixarenes have also been investigated to act as a phosphodiesterase enzyme models (13-15). Calixarenes with group containing nitrogen and sulfur atoms are also found as an ion-selective electrode sensitive to soft heavy metal ions such as Ag<sup>+</sup>, Pb<sup>2+</sup> and Hg<sup>2+</sup> (16–22). Calixarene can be functionalized with phosphines, amides and imines. They come under attractive category that acts as host molecule for transition metal ions and for the formation of supramolecular building blocks (23, 24). The bis-(8-oxyquinoline)calix[4]arene, Di-aza-benzo crown ether derived from p-tert-butyl calix[4] arenes species is known to be effective receptor for Zn<sup>2+</sup> ions (25, 26). Calix[6]arene-based receptor with hydrophobic imidazole cavity displays a remarkable set of biomimetic properties and binds with Zn<sup>2+</sup> ion (27, 28).

Herein this paper, we report synthesis and metal cation binding properties of bis-formylpyrazole calix[4]arene derivative. The lower rim functionalization of calixarene with pyrazole has been chosen to design a moiety with the effective electron density. Oxygen and nitrogen atoms in calixarene are efficient to bind with Zn<sup>2+</sup> ion.

#### 2. Experimental

#### 2.1. Chemicals and reagents

All reagents and solvents were obtained from CDH, Spectrochem, Merck and Sigma Aldrich. The reagents and solvents were used without further purification. Thin-layer chromatography was performed on silica gel 60 F254 silica-aluminium plates, and the plates were visualized using ultraviolet light.

#### 2.1.1. Instruments

The glasswares were dried overnight in an oven before use. Open capillaries were used to determine melting point and are thus uncorrected. IR spectra were recorded on ABB MB 3000 IR Spectrophotometer. NMR data were recorded on a Bruker AV(III)-400 MHz, with a BBFO probe. All samples were analysed in CDCl<sub>3</sub>. The reference values for the residual solvent (CDCl<sub>3</sub>) were taken as  $\delta$  = 7.27 ppm for <sup>1</sup>H-NMR and  $\delta$  = 77.1 ppm for <sup>13</sup>C-NMR. The multiplicities for the coupled signals were designated using the following abbreviations: s = singlet, d = doublet, m = multiplets and are given in hertz. Mass spectra were recorded on a Xevo G2-S Q-T of spectrometer (Waters, USA), capable of recording high-resolution mass spectrum in the electrospray ionisation (ESI) modes.

#### 2.2. Synthesis of receptor DPPMACA

4-formylpyrazole 4 was synthesised by the reported procedure (29). The calix[4] arene hydrazone 5 was synthesised by reported procedure (30, 31) (Scheme 1). The lower rim substituted bis-formylpyrazole calix[4]arene derivative DPPMACA was synthesised by refluxing 5 (0.8827 mmol) with formylpyrazole (1.7654 mmol) as in 1:2 M ratio in ethanol with 2-3 drops of glacial acetic acid as catalyst for 30 h (Scheme 2). After product formation as observed by TLC in methanol-chloroform solvent system; the reaction mixture was cooled at room temperature and precipitated with the yield of 70%. The solid obtained was recrystallized with methanol-chloroform. The precipitate was filtered with whatman filter paper 41, dried in vacuum oven and subjected to spectral analysis (IR, <sup>1</sup>H NMR (Figure S1, Figure S2), <sup>13</sup>C NMR (Figure S3) and mass spectroscopy (Figure S4). Melting point 250 °C; IR( $v_{max,}$  cm<sup>-1</sup>): 3257, 2958, 1699, 1598, 1544, 1485, 1444, 1357, 1296, 1209, 1055, <sup>1</sup>H NMR:  $\delta$  (ppm) 11.37 (s, 2H, N**H**, D<sub>2</sub>O exchangeable), 8.79 (s, 2H, pyrazole-H), 8.66-8.62 (d, 4H, Ar-H), 8.43 (s, 2H, CH=N),



Scheme 1. (i) ethanol-water acetic acid cat. (ii) POCI3/DMF, 50–60 °C, 5–6 h.



Scheme 2. (iii) ethanol/acetic acid cat/refluxed, 30 h.

8.22 (s, 2H, O**H**, D<sub>2</sub>O exchangeable), 7.84–7.73 (m, 4H, Ar**H**), 7.66–7.64 (d, 2H, Ar–H), 7.54–7.44 (m, 6H, Ar–H), 7.40–7.31 (m, 4H, Ar–H), 7.14, (s, 4H, Ar–H), 6.92(s, 4H, Ar–H), 4.19 (s, 4H,  $-OCH_2$ –), 3.86–3.82 (d, 4H,  $-Ar-CH_2$ –Ar–), 3.39–3.35 (d, 4H,  $-Ar-CH_2$ –Ar–), 1.33(s, 18H,  $-CH_3$ ), 1.05(s, 18H,  $-CH_3$ ). <sup>13</sup>C NMR (75 MHz, CDCl3):  $\delta$ (ppm); 182.75, 132.00, 129.57, 128.95, 128.81, 128.75, 128.81, 128.75, 125.190, 119.42, 119.34, 117.20, 78.12, 77.34, 76.71, 34.18, 31.62, 30.94. MS-ESI-TOF (m/z) for C<sub>80</sub>H<sub>84</sub>N<sub>8</sub>O<sub>6</sub> Calcd: 1252.6513 (M); Found: 1253.2372 (M + 1)<sup>+</sup> (Figure S4).

#### 2.3. Computational methodology

The Geometry were optimised using Gaussian at density functional level (DFT) B3LYP/6-31G\* of theory (*32*). The Visualization of prior Geometry optimised structure and Geometry optimised structure were done using Schrodinger suite. The optimised structure was used as starting host (DPPMACA) and Zn<sup>+2</sup> as a guest for docking in Hex 8.0 software (*33*).

The Fast Fourier transformation algorithm of rigid DPPMACA approached with spherical polar Fourier basis functions and grid sampling was accomplished to evolve the 1D, 3D and 5D orientations. The computational analysis was carried out to emphasise the best pair wise interactions between the host and guest molecules through rotational correlation over angular terms in a constrained search space approach. The inclusion complex of host and guest was utilized for the superimposition to decipher the 3D knowledge based shapes energy scores calculation. Thereafter, the best docked pose was retrieved from the top ten scored clusters. The lowest energy pose was taken as an input for Molecular dynamics stimulation using the Desmond Program version (academic version) (*34, 35*).

To build the system, simple Point Charge water was preferred as a solvent with optimisation potential for liquid simulation, all atoms force field 2005 (36) in the cubic periodic box  $(10 \times 10 \times 10)$  size followed by neutralisation process through Na<sup>+</sup> and Cl<sup>-</sup> counter ions. The docked host-quest complex was selected with 5036 atoms and 1619 water molecules proceeded by restraining steps through system minimisation and pre-equilibrium to relax the system initially. Ten nanosecond time interval was chosen for the molecular dynamic (MD) simulations with relaxation time of 2 ps at constant temperatures of 300 K, pressure 1.03215 bar with Nose-Hoover thermostat and Martyna-Tobias-Klein Barostat method having constant volume and shape ensemble (NVT). In the simulation process, Smooth Particle Mesh Ewald method (37) (with a 10<sup>-9</sup> tolerance limit) was employed to decipher the long range electrostatic interactions along with short-range cut-off distance of 9.0 A (*37*), and long range electrostatic interactions. For detailed analysis, 1000 frames were generated during 10 ns in the trajectory and captured every 10 ps time step. Furthermore, the structural changes and dynamics behaviour of the complex were investigated by estimating the root mean square deviation (RMSD), total energy (*E* Total).

The Becke 3-parameter exchange functional together with the Lee–Yang–Parr correlation functional (B3LYP) (*38*, *39*) was used for all the calculations in the density functional theory (DFT) method. In some previous reports, The B3LYP functional has been successfully utilized for geometry optimisation of transition metal complexes (*40–43*). The general basis sets were used for the complex DFT calculation. The [B3LYP/6-31+G(d-p)/LANL2DZ] LANL2DZ relativistic pseudopotential was used for the zinc metal ion, while the C, H, N, O and S atoms were described by the 6-31+G(d-p) (*43–45*). The DPPMACA and metal complexes were demonstrated using Avogadro version 1.2.0 software (*46*). The gas phase geometry optimizations were carried out without symmetry constraint by using the Gaussian 09 W software (*32*).

The electronic structure calculations, thermodynamic parameters were obtained from the geometry optimised structure. The frontier molecular orbital (FMO) energies, the energy of the lowest unoccupied molecular orbitals ( $E_{LUMO}$ ) and the energy of the highest occupied molecular orbital ( $E_{HOMO}$ ), of the studied metal complexes are calculated. The absorption spectra calculated using TD-DFT level of theory. The effect of solvent (THF) was systematically monitored for all the steps via conductor-like Polarizable Continuum Model (CPCM).

## **2.4.** General procedure for the detection of cations by spectrophotometry

Stock solutions of DPPMACA (10 µM) and the sulphate salts (10 μM) of various metal ions [Zn<sup>2+</sup>, Y<sup>3+</sup>, Eu<sup>3+</sup>, Dy<sup>3+</sup>, Na<sup>+</sup>, Nd<sup>3+</sup>, Fe<sup>2+</sup>, Cd<sup>2+</sup>, Al<sup>3+</sup>, Be<sup>2+</sup>, La<sup>3+</sup>, Cu<sup>2+</sup> and K<sup>+</sup> ions] were prepared in THF-H<sub>2</sub>O (1:1 v/v) as the solvent system. In a 5-mL volumetric flask, 2.5 mL of the DPPMACA solution and 2.5 mL of metal salt stock solutions were combined so that the effective concentrations of both DPPMACA and metal ions were same. Absorption studies were performed using the as prepared solutions. A Job's plot (Figure 4) and Benesi-Hildebrand plot (Figure 5) were also performed based on the absorption studies to establish the stoichiometry and association constant of receptor-metal. UV/ VIS spectra (electronic spectra) of receptor and metal ions with receptor were recorded on T 90 (PG Instruments Ltd) UV/VIS spectrometer in the region 700-200 nm THF:H<sub>2</sub>O solvent system.

#### 3. Result and discussion

#### 3.1. Evaluation of DPPMACA for ionic recognition

The synthesised molecular receptor DPPMACA was evaluated for cation binding ability by UV-visible spectroscopy using THF-water as solvent. The titration of receptor DPPMACA were carried out in THF:H<sub>2</sub>O (1:1 v/v) by adding sulphate salts of Zn<sup>2+</sup>, Y<sup>3+</sup>, Eu<sup>3+</sup>, Dy<sup>3+</sup>, Na<sup>+</sup>, Nd<sup>3+</sup>, Fe<sup>2+</sup>, Cd<sup>2+</sup>, Al<sup>3+</sup>, Be<sup>2+</sup>, La<sup>3+</sup>, Cu<sup>2+</sup> and K<sup>+</sup> metal ions (Figure 1). The UV-Vis absorption spectrum of the receptor DPPMACA (10  $\mu$ M) exhibits absorption bands at  $\lambda_{max'}$  230 and 280 nm, respectively (Figure 1). There was a negligible response upon the addition of Y<sup>3+</sup>, Eu<sup>3+</sup>, Dy<sup>3+</sup>, Na<sup>+</sup>, Nd<sup>3+</sup>, Fe<sup>2+</sup>, Cd<sup>2+</sup>, Al<sup>3+</sup>, Be<sup>2+</sup>, La<sup>3+</sup>, Cu<sup>2+</sup> and K<sup>+</sup> metal ions as their sulphate salt. When Zn<sup>2+</sup> ions was added to receptor DPPMACA then a bathochromic shift was observed in absorption spectra of receptor DPPMACA from 280 to 294 nm, 230 to 244 nm and a decrease in absorbance with isobestic point 261 and 237 nm. Upon addition of Zn<sup>2+</sup> ions to a solution of receptor DPPMACA, a decrease in absorbance and shifting in absorption maxima was noticed due to interaction of Zn–O and Zn–N of lower rim calixarene (Table 1). Phenolic and pyrazole group present in calixarene shows



Figure 1. (Colour online) UV-vis spectra of receptor DPPMACA (10  $\mu$ M) with Zn<sup>2+</sup>, Y<sup>3+</sup>, Eu<sup>3+</sup>, Dy<sup>3+</sup>, Na<sup>+</sup>, Nd<sup>3+</sup>, Fe<sup>2+</sup>, Cd<sup>2+</sup>, Al<sup>3+</sup>, Be<sup>2+</sup>, La<sup>3+</sup>, Cu<sup>2+</sup> and K<sup>+</sup> used as their sulphates in THF:H<sub>2</sub>O (1:1 v/v) as solvent system.

Table 1. Docking result analysi	Table	1. Docking	result ana	lysis
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No	Interaction of molecule	Name of interaction	Distance (Å)
1	Zn–O	Metal-Acceptor	2.41
2	Zn–O	Metal-Acceptor	2.15
3	Zn–O	Metal-Acceptor	1.87
4	Zn–O	Metal-Acceptor	1.85
5	Zn–N	Metal-Donor	1.65

absorption spectra at 280 nm band due to  $\pi - \pi^*$  transition in both rings.

The effect of different metal ions with respect to zinc metal ion was also checked at the same concentration (Figure 2) (47). The results showed that the presence of other metal ions (Y<sup>3+</sup>, Eu<sup>3+</sup>, Dy<sup>3+</sup>, Na<sup>+</sup>, Nd<sup>3+</sup>, Fe<sup>2+</sup>, Cd<sup>2+</sup>, Al<sup>3+</sup>, Be<sup>2+</sup>, La<sup>3+</sup>, Cu<sup>2+</sup> and K<sup>+</sup>) with Zn<sup>2+</sup> metal ions had a minimal effect on the absorption spectra of DPPMACA + Zn<sup>2+</sup> ions.

Also UV-vis titration was carried out; gradual addition of Zn<sup>2+</sup> ions (0–5 equivalent) led to a decrease in absorbance of band at 280 and 230 nm with appearance of a new band at 294 and 244 nm and an isosbestic points at 261 and 237 nm (Figure 3). The formation of inferred isosbestic points indicated that a new species was formed and the



**Figure 2.** (Colour online) Observed interference study of the metal cations (Y<sup>3+</sup>, Eu<sup>3+</sup>, Dy<sup>3+</sup>, Na<sup>+</sup>, Nd<sup>3+</sup>, Fe<sup>2+</sup>, Cd<sup>2+</sup>, Al<sup>3+</sup>, Be<sup>2+</sup>, La<sup>3+</sup>, Cu<sup>2+</sup> and K<sup>+</sup>) with DPPMACA + Zn<sup>2+</sup> ions (10  $\mu$ M) in THF: H<sub>2</sub>O (1:1 v/v) as solvent system at same concentration.



**Figure 3.** (Colour online) UV-vis spectra of receptor DPPMACA (10  $\mu$ M) with increasing concentration of Zn<sup>2+</sup> ions in THF: H<sub>2</sub>O (1:1 v/v) as solvent system.

transition between the free and the complexed species in the solution. It was envisioned that the synthesised cavity derived from diphenyl-pyrazolyl might be of 1:1 stoichiometry of DPPMACA:Zn<sup>2+</sup> ions, indicating an equilibrium between DPPMACA and its Zn<sup>2+</sup> complex THF: H<sub>2</sub>O (1:1 v/v) as solvent system (48). The Job's plot (Figure 4) and Benesi-Hildebrand plot (Figure 5) reveals the formation of a complex between DPPMACA and Zn<sup>2+</sup> ions with 1:1 stoichiometry (49, 50). Also complexation of DPPMACA-Zn<sup>2+</sup> was determined by MS-ESI spectroscopy DPPMACA (MS-ESI-TOF (m/z) for C<sub>80</sub>H<sub>84</sub>N<sub>8</sub>O<sub>6</sub> Calcd: 1252.6513 (M); Found: 1253.2372 (M + 1)<sup>+</sup> (Figure S4) and MS-ESI-TOF (m/z) for DPPMACA-Zn<sup>2+</sup> complex found 1314.1831and m/z 1253.1522 for DPPMACA (Figure S5). Mass spectroscopy is found to be in good agreement with the proposed structures of receptor DPPMACA-Zn<sup>2+</sup> complex. The mass



**Figure 4.** (Colour online) Job plot for DPPMACA-Zn<sup>2+</sup> complex in THF-H<sub>2</sub>O (v/v = 1/1) solvent system. ([DPPMACA] + [Zn<sup>2+</sup>]) =  $20 \times 10^{-6}$  M at  $\lambda$ max = 280 nm.



**Figure 5.** (Colour online) B-H plot at 280 nm of receptor DPPMACA and  $Zn^{2+}$  ion. Using Benesi–Hildebrand method employing 1/  $(A - A_o) = 1/(A - A_f) + 1/K(A - A_f)[Zn^{2+}]$  equation and observed linearity in the plot which indicated the formation of a 1:1 complex with association constant  $6.438 \times 10^3 \text{ M}^{-1}$ .

study of complexation is evident for 1:1 complexation of the DPPMACA-Zn<sup>2+</sup>. The binding affinity, which was calculated by the Benesi–Hildebrand using the absorption spectra found to be  $6.438 \times 10^3$  M<sup>-1</sup>.

#### 3.2. Docking

Geometry optimisation (Figure 6) was carried out through the Gaussian 09 program package and Figure 7 confirms the optimisation steps with energy fluctuation. Molecular docking was performed to evaluate the binding mechanism of DPPMACA complex with zinc metal ion to correlate the quenching mechanism. Figure 8 shows the top



Figure 6. (Colour online) Geometry optimised image of DPPMACA.



Figure 7. (Colour online) DPPMACA geometry optimisation graph.



Figure 8. (Colour online) Molecular docking posese of DPPMACA\_Zn<sup>2+</sup> complex.

view as well as front view of docked complex. The Zn<sup>2+</sup> molecules were reacted as a guest which bound with the host (DPPMACA). Five significant interactions (Table 1) were identified by docking analysis and four of them were metal acceptor while 1 was metal donor within the range of 1.65–2.41 Å (Table 1). The docked compound remained in the centre of the host compound which was the main aspect of the binding with metal acceptor groups. So, these results show the detection of metal ion with host compound. Figure 4 Different views allowed to decipher the binding affinity of Zn<sup>2+</sup> compound with selected target very deeply.

#### 3.3. Molecular dynamics

Molecular dynamics (MD) simulations were implemented to gauge the structural stability and integrity of hostguest inclusion complex for 10 ns time trajectories. MD simulations were executed in water solvent with constant shape and volume at room temperature to understand the behaviour and interactions of host-guest inclusion complex during the whole event which reveals the total energy, potential energy, temperature, volume, pressure, RMSD, root mean square fluctuations, intramolecular H-bond and radius of gyration (rGyr) at various time trajectories (Figure S8).

The average total energy value, potential energy value was given in Table 2. Figure 9 shows the event analysis of host-guest inclusion complex after the completion of MD simulation event which clearly depicts the major fluctuation in volume parameter within the range of 50,000-52,000 value while rest of all remained in between -204.861 and 500 value range. Different types of energies were obtained from event analysis, ranging from -200 to 500 kcal/mol which shows the changes occurred during the whole event were consolidated by the aforesaid range to make the complex stable. The most structural change was notified in RMSD values which had not affected the confirmation of host-guest inclusion complex and the average range was 0.75 to 4.8 Å. After the 9 ns time interval the drastic change was observed in the confirmation of host-guest inclusion complex with the decreased numbers of RMSD values. Intra-hydrogen bonds were found during whole event that supports binding mechanism. Event analysis energy value during 0-10 ns has been calculated.

Table 2. Simulation quality analysis result.

	Average	SD	Slope (ps <sup>-1</sup> )
Total energy (kcal/mol)	-13014.535	47.058	-0.000
Potential energy (kcal/mol)	-16032.925	36.867	-0.000
Temp.(K)	298.793	1.732	0.000
Pressure (bar)	-8.149	127.687	0.001
Volume (cm <sup>3</sup> )	51429.914	137.616	0.001

Furthermore, a steady RMSD trajectory value with a small change in the position in the Zn<sup>2+</sup> atoms clearly specified that the stability of the complex throughout the length of the simulation run. No major fluctuations in the rGyr, MolSA, SASA, and PSA plots were detected, which again established the compactness and steady exposure of Zn<sup>2+</sup> for a favourable conformational cavity of the DPPMACA (Figure S9, Figure S10).

#### 3.4. DFT calculation

Absorption spectra at the TD-DFT level of theory:

The nature of the absorption spectra was highlighted via the quantum mechanical studies based on TD-DFT. Experimental and theoretical lowest energy transitions  $(\lambda_{max})$  were perceived by analysing the nature of these transitions from the topologies of the Kohn–Sham orbitals. The FMO's of DPPMACA can be found in Figure 8, and the maximum wavelength absorption  $(\lambda_{max})$  is presented in Table 3. It was clearly observed (Figure 10) that the UV spectra emerged due to the electronic transitions from an amalgam of higher energy orbitals (HOMO-19, HOMO-10, HOMO-3, and HOMO) to lower energy orbitals (LUMO+1). Note that HOMO and LUMO was distributed on moiety substituents of DPPMACA. During the transitions, the distributions of LUMOs were not considerably affected even for other excited states. The significant electronic conjugation



Figure 9. (Colour online) Root mean square deviation (RMSD), radius of gyration (rGyr), molecular surface srea (MolSA), solvent accessible surface area (SASA), and polar surface area (PSA) of the complex over a time period of 10 ns.

Sr. no.	Name	Excitation (eV)	$\lambda_{ m excitation}$	Oscillator strength	Key transitions	% Contribution	$\lambda_{exp}$
1	DPPMACA	4.3858	282.7	0.9379	HOMO-19→HOMO	2.03	280
					HOMO-10→HOMO	9.90	
					HOMO-3→HOMO	51.92	
					HOMO-1→LUMO+1	21.93	
2	DPPMACA_Zn	4.1903	296.57	0.1033	HOMO-5→LUMO+6	2.74	294
					HOMO-2→LUMO	5.20	
					HOMO-2→LUMO+1	24.16	
					HOMO-2→LUMO+2	4.01	
					HOMO-2→LUMO+3	10.42	
					HOMO-2→LUMO+6	25.69	
					HOMO-2→LUMO+15	2.55	
					HOMO→LUMO+6	2.02	

**Table 3.** Main singlet vertical electron transition energies ( $\Delta E$ ), wavelengths ( $\lambda$ ), oscillator strengths (f), and calculated at the TDDFT/ CAMB3LYP level.



**Figure 10.** (Colour online) Molecular orbital representation of receptor (DPPMACA) obtained at the CPCM-TD-cam-b3lyp/6-31+G(d-p) level of approximation.

between calixarene and moiety (DPPMACA\_Zn) is mainly due to the shifting of the electron density from HOMO-1 to LUMO+1 in the first excited state. However, other transitions were also possible that originated from HOMO and other lower energy orbitals. Also, the FMO of DPPMACA complex with Zn metal ion depicted in Figure 11, maximum wavelength absorption ( $\lambda$ max) is presented in Table 1. It was perceived that the UV spectra emerged due to the electronic transitions from an amalgam of higher energy orbitals (HOMO-5, HOMO-2, and HOMO) to lower energy orbitals (LUMO, LUMO+1, LUMO+2, LUMO+3, LUMO+6, and LUMO+15) (Figure 11). It was clearly identified that the UV-vis spectra of DPPMACA gives a bathochromic shift of 14 nm with Zn<sup>2+</sup> metal ion due to complexation. The oscillator strength of these transitions was found to be feeble due to the non-bonded nature of the complex.



Figure 11. (Colour online) Molecular orbital representation of DPPMACA complexed with Zn metal obtained at the CPCM-TD-camb3lyp/6-31+G(d-p) level of approximation.

#### 4. Conclusion

In this paper an investigation was carried out to determine the probability of DPPMACA as a receptor for Zn<sup>2+</sup> ions. The synthesised Bis-(1,3-diphenyl-pyrazolyl methylene acetohydrazide)Calix[4]arene (DPPMACA) has been characterised by various spectral methods and it shows strong recognition potential for Zn<sup>2+</sup> ions on evaluation with several metal sulphates. The stoichiometry was found to be 1:1 with stability constant  $6.438 \times 10^3$  M<sup>-1</sup>. The host guest interaction was also determined by computational methodology, molecular dynamics and DFT calculations.

Although many techniques are available for the determination of  $Zn^{2+}$  but due to easiness in handling, low cost, good sensitivity, reliability and availability of instruments, the spectrophotometry gains popularity over other techniques. Computational discernments were provided to understand the interaction behaviour/mechanism of DPPMACA with  $Zn^{2+}$  ions via molecular docking followed by dynamics studies.  $Zn^{2+}$  was stabilized by the non-covalent interaction achieved by the cavity of DPPMACA. Importantly, the electronic transitions observed in the excitation spectrum were generated from the shifting of the electron density of HOMOs to LUMOs of  $Zn^{2+}$  to distribute at the arms of the DPPMACA. The proposed method using DPPMACA is highly qualified for determination of zinc. Further a method can be developed as a new, simple, sensitive and selective approach for the determination of  $Zn^{2+}$  ions in real samples.

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#### **Disclosure statement**

No potential conflict of interest was reported by the authors.

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