INVESTIGATION STUDY OF TRANSITION STATE FOR SYNTHESIS NEW SCHIFF BASE LIGANDS OF ISATIN DERIVATIVES

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ABSTRACT

Quantum calculation methods have been used to estimate the real transition states of synthesis new Schiff base ligands derivative from Isatin using semiemperical calculation methods. Optimized structures and vibration spectrum have been calculated to the prepared compounds, that's compared with their practical data. Theoretical study of transition states have been done to investigate the real transition state of reaction through zero point energy, total binding energy and first imaginary frequency. Three suggested transition states have been proposed into the reaction of 4-DMIA with 2-hydroxy amine. They found the second transition state is real transition state than other proposed, due their energetic values. Suggestion of six transition states to the reaction of DMAA with Isatin. Good agreements has been found between the experimental and theoretical data for the synthetic products, likes[(3E)-3-[3-(2-hydroxy phenylimino)-1,5-dimethyl-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino]indolin-2-one] and [(3E)-3-[3-(3-amino phenylimino)-1,5-dimethyl-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino]indolin-2-one] as final products.

Key words: Quantum calculation methods, Transition states, Isatin, Schiff base, Semi-empirical and PM3.

INTRODUCTION

Biological activities are released by Schiff bases derivatives from Isatin such as antifungal, antiviral, and anticancer, due to cis-α-dicarbonyle moiety of Isatin[1-4]. Schiff bases specially poly dentate with deferent donor atoms such as (N_2O_2, NNNN, ONO)[5-7], which made these compounds good substrate for the synthesis of metal complexes either alone or

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mixed with different other ligands[8]. Schiff base ligands have wide range of application[9]. In analytical chemistry along record of use as chromogenic reagent for determination of many metals including Ni(II) in some natural food samples[10]. Importance of these compounds is come out by presence of azomethine group, which plays an important role in coordination[11].

The tools of computational chemistry have been used to investigate the chemical behavior and different reactivity parameterized of synthetic derivatives[12,13]. Chemical synthesis reactions required optimized structures of their chemical species and their transition states of synthesis reaction. The structural properties are elementary keys to understand the chemical reactivity during the potential energy surface calculations[14,15].

In present work, the transition state of synthesis reaction for Schiff's base compound using different conditions and reactant species has been carried out. Simulation studies are taken in several stages of calculation. To estimate at the last spectroscopic comparative study, that's made and suggested the real transition state for the reaction.

EXPERIMENTAL

Materials and methods

All chemicals used were supplied from BDH, Fluka, and Merck companies and used without any further purification Absorption spectra were recorded using Shimadzu UV-Vis 1700 spectrophotometer, for solution of the complexes in aqueous ethanol at room temperature. Using 1 cm quartz cell. IR spectra were recorded with FT-IR-8000 Shimadzu, in the range of (4000-400) cm^{-1} using KBr discand melting points were obtained using an electro thermal apparatus Stuart melting point.

Calculation details

Semi-empirical methods according to molecular orbital theory have been used to find the optimized structures of (4-DMIA) and (DMAA) and their Schiff base derivatives structural configuration interaction (2X 2) of microstate. The transition state for the reaction path techniques have been studied using quadratic synchronous transit method (QST) of hyperchem 8.02[16]. It searches for a maximum along a parabola connecting reactants and products, and for a minimum in all directions perpendicular to the parabola. Vibration frequencies of the proposed transition state structures have been calculated at UHF/PM3 for characterization of the nature of zero point energy (ZPE) calculations to compute the quantum energies of these reactions.

Preparation of Schiff base (3E)-3-[(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)imino]-1,3-dihydro-2H-indol-2-one (4-DMIA)

In a round bottom flask, 4-aminoantipyrine (0.01 mol, 2.03 g) in (15 mL) ethanol and Isatin (0.01 mol, 1.47 g) in (15 mL) ethanol added few drops of glacial acetic acid to solution the mixture was refluxed for (6 hr), the product precipitate was obtained by filtration and recrystallized from hot ethanol, and dried over anhydrous $CaCl_2$.[17]

Preparation of schiff base N-(4-amino-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-ylidene)-N-(3-aminophenyl)amine (DMAA)

In a round bottom flask, 4-aminoantipyrine (0.01 mol, 2.03 g) in (15 mL) ethanol and (0.01 mol, 1.08 g) of 3-phenylene di amine in (15 mL) ethanol added few drops of glacial acetic acid to solution the mixture was refluxed for (10 hr), the product precipitate was obtained by filtration and recrystallized from hot ethanol and dried over anhydrous $CaCl_2$.

Preparation of new schiff base ligand (2-HDMIA)

The Schiff base ligand (2-HDMIA) was prepared by condensation of compound (4-DMIA) (0.01 mol, 3.32 g), which was dissolved in (50 mL) ethanol and refluxed with (0.01 mol, 1.09 g) of 2-hydroxy amine for (16 hr)[18]. Adding three drops from glacial acetic acid, a clear colored solution was obtained. The Schiff base ligand was isolated after the volume of mixture was reduction to half by evaporation and recrystallized by hot ethanol and dried over anhydrous $CaCl_2$.

Preparation of new schiff base ligand (3-ADMIA)

The Schiff base ligand (3-ADMIA) was prepared by condensation of compound (DMAA) (0.01 mol, 2.933 g), which was dissolved in (50 mL) ethanol and refluxed with Isatin (0.01 mol, 1.47 g) in (15 mL) for (30 hr)[19]. Adding three drops from glacial acetic acid, a clear colored solution was obtained. The Schiff base ligand was isolated after the volume of mixture was reduction to half by evaporation and recrystallized by hot ethanol and dried over anhydrous $CaCl_2$.

RESULTS AND DISCUSSION

Fig. 1 shows the geometries of the only possible three proposed transition state structures. These have been optimized and (4-DMIA) was IR-tested. The probable transition state of prepared compounds comes out through confirmation Table 1. It shows the

interaction of (4-DMIA) with (2-hydroxy amine) in transition state, which are expected to yield TS2 is the real transition state and second transition state is the most probable state to give up the reaction products than other states due to the highest value of zero point energy 216.243 kCal mol^{-1} and highest energy stability -93552.470 kCal mol^{-1}.
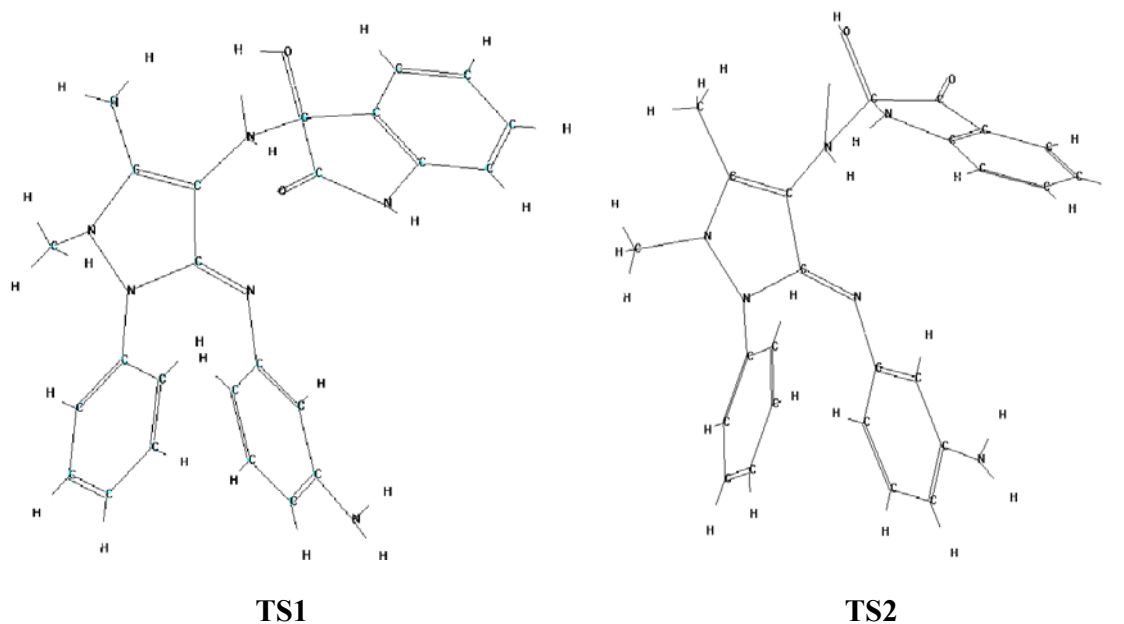

TS1   **TS2**

TS3
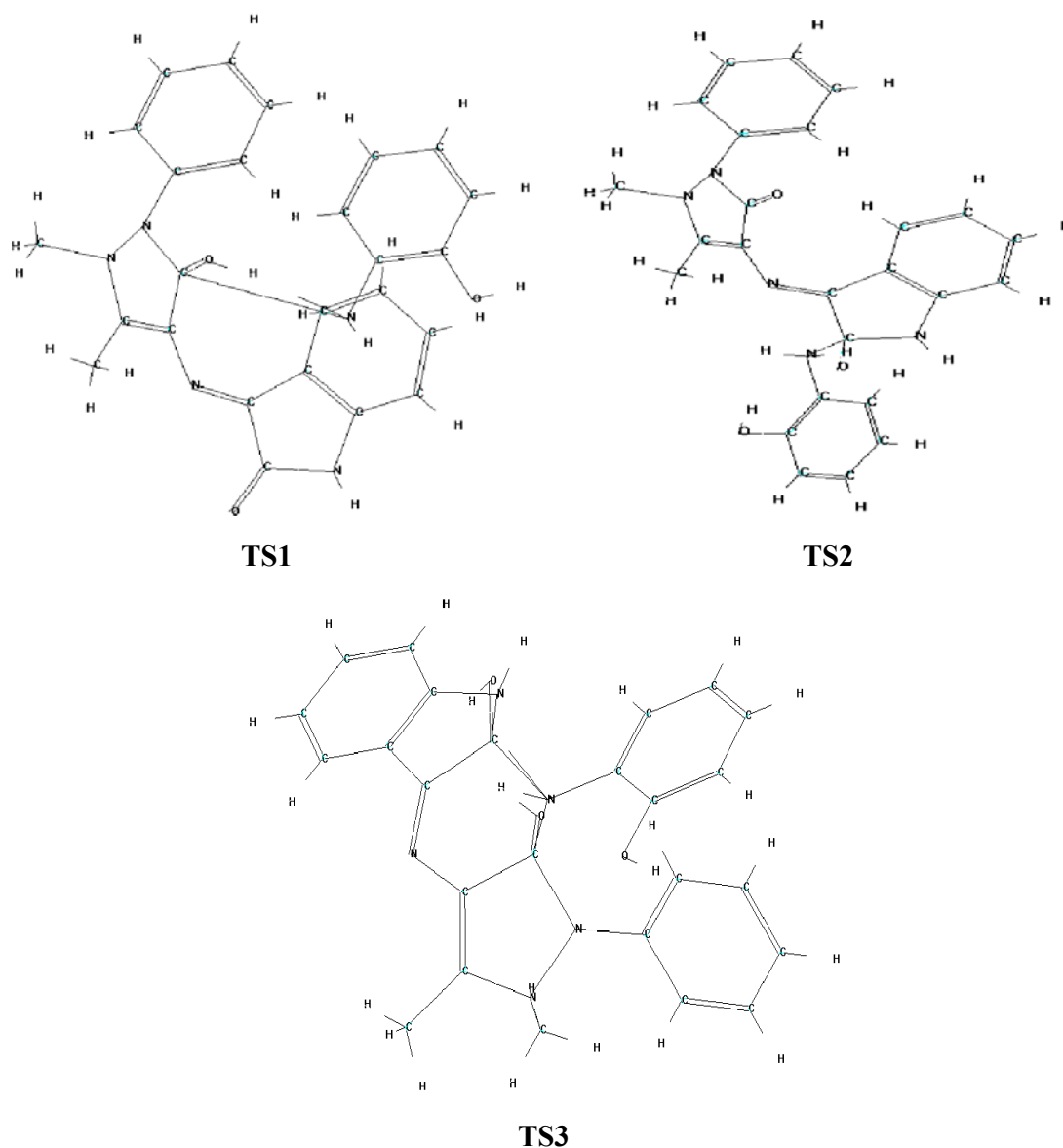
Fig. 1: Geometrical wire form view of proposed transitions states calculated at UHF/MP3 of 2-HDMIA

Table 1: Energy properties of probable transition states for 4-DMIA with 2-hydroxyamine calculated at UHF/PM3

Transition state	Total energy (KCal/mol)	Binding energy (KCal/mol)	Zero point energy (KCal/mol)	IR-Frequency (Imaginary)	Heat of formation (KCal/mol)
S1	-93499.664	-4780.168	213.804	-	35.254
S2	-93552.470	-4832.975	216.243	-	-17.552
S3	-93449.4	-4729.9	209.833	-	85.52

Fig. 2 shows the geometries of the six proposed transition state structures. These have been optimized and (DMAA) was IR-tested. The probable transition state of prepared compounds comes out through confirmation Table 2. It shows the interaction of (DMAA) with Isatin in transition state, which are expected to yield TS1 is the real transition state and first transition state is the most probable state to give up the reaction products than other states due to the highest value of zero point energy 283.923 kCal mol^{-1} and highest energy stability -112774.114 kCalmol^{-1}.[16]

TS1   TS2

Cont…

TS3

TS4

TS5

TS6
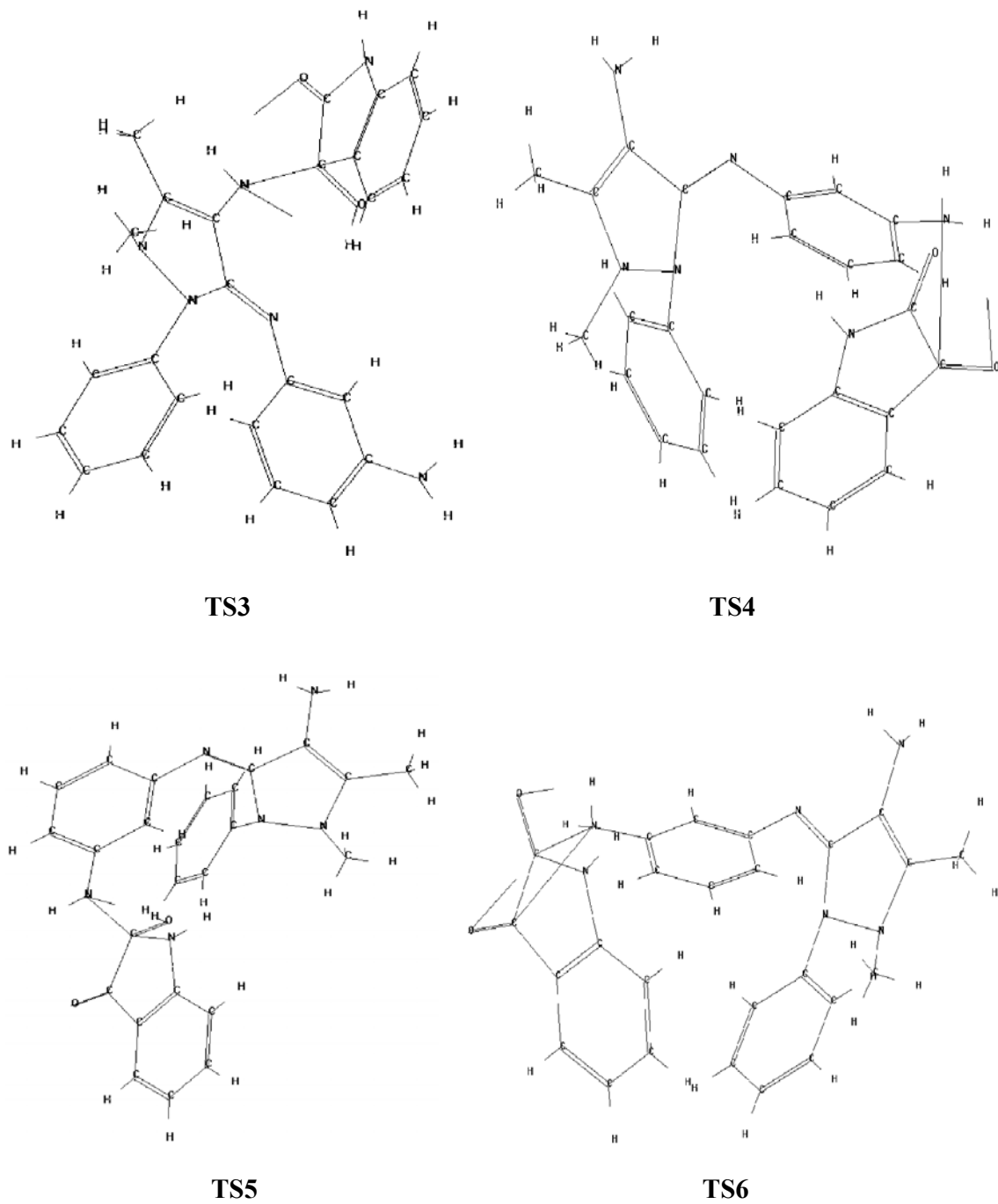
Fig. 2: Geometrical wire form view of proposed transitions states calculated at UHF/MP3 of 3-ADMIA

Table 2: Energy properties of probable transition states for DMAA with Isatin calculated at UHF/PM3

Transition state	Total energy (KCal/mol)	Binding energy (KCal/mol)	Zero point energy (KCal/mol)	IR-Frequency (Imaginary)	Heat of formation (KCal/mol)
S1	-112774.114	-6258.353	283.923	-	61.462
S2	-112773.114	-6257.353	283.563	-	62.462
S3	-112773.392	-6257.631	283.252	-	62.184
S4	-112768.693	-6252.932	277.751	-	66.883
S5	-112772.911	-6257.150	279.350	-	62.665
S6	-112771.304	-6255.543	277.519	-	64.272

Table 3 shows comparison between the experimental and theoretical vibration spectrum of the synthetic compounds.

Table 3: Comparative of experimental and theoretical vibration spectrum analysis of synthetic compounds

Compound	Experimental cm^{-1}	Theoretical $PM3/cm^{-1}$	Intensity	Description
(3-ADMIA)	3394	3487	90586.860	N-H Asymmetric
	3364	3344	12055.210	N-H symmetric
	1653	1643	4163.225	C=N1
	1618	1569	4315.949	C=N2
	1718	1763	9732.004	C=O
	3064	3100	9307.601	C-H Ar
	2922	2999	10704.170	$N-CH_3$
	1492	1497	1593.685	C=C
(2-HDMIA)	3402	3642	235	O-H
	1663	1665	57	C=N2
	1616	1647	34	C=N1
	1718	1819	111	C=O
	3064	3014	2297	C-H Ar
	1595	1512	662.067	C=C

        The compound (3-ADMIA) was confirmed according to data. They found in good
agreement by two bands at 3394 cm^{-1} and 3364 cm^{-1} due to asymmetric and symmetric
stretching vibrations of ν NH$_2$ group, respectively. Absorption bands at 2922 cm^{-1}was
attributed to N-CH$_3$ group. Bond absorption at 1653 cm^{-1} and 1618 cm^{-1} was due to ν C=N
stretching. The sharp bands at 1591 is due to the ν C=C stretching vibration. The compound
(2-HDMIA) was confirmed according to data, they found in good agreement[20]. Absorption
band of O-H group found at 3402 cm^{-1}. Bond absorption at 1663 cm^{-1} and 1616 cm^{-1} was
due to ν C=N stretching. The sharp bands at 1595 is due to the ν C=C stretching vibration as
showed in Figs. 2, 3, 4 and 5.
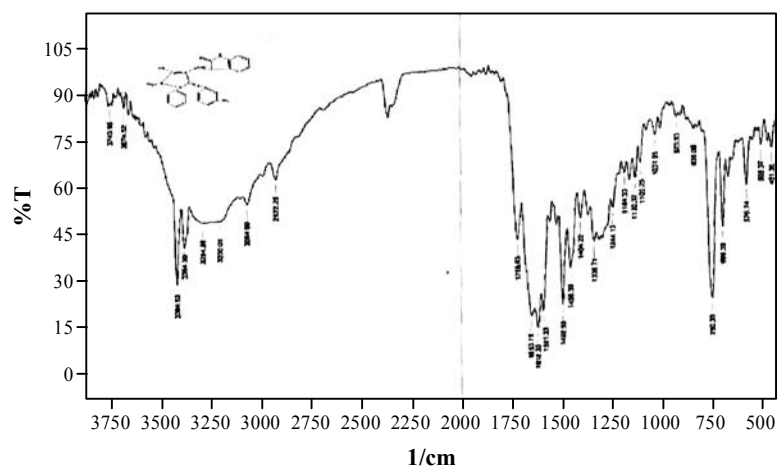
Fig. 2: Experimental FTIR vibration spectra of 3-ADMIA
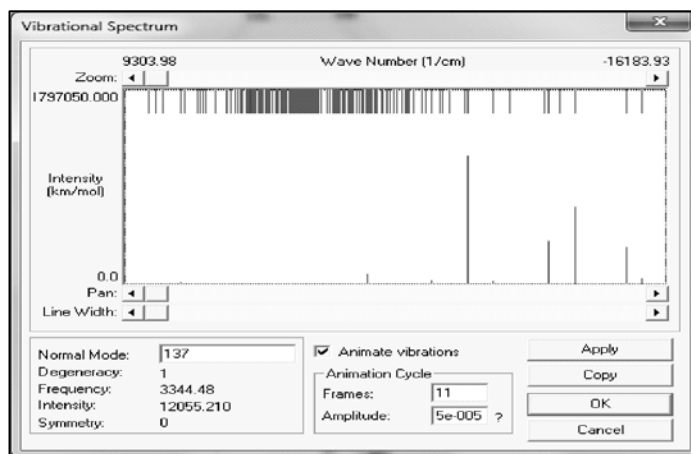
**Fig. 3: Theoretical FTIR vibration spectra of 3-ADMIA**
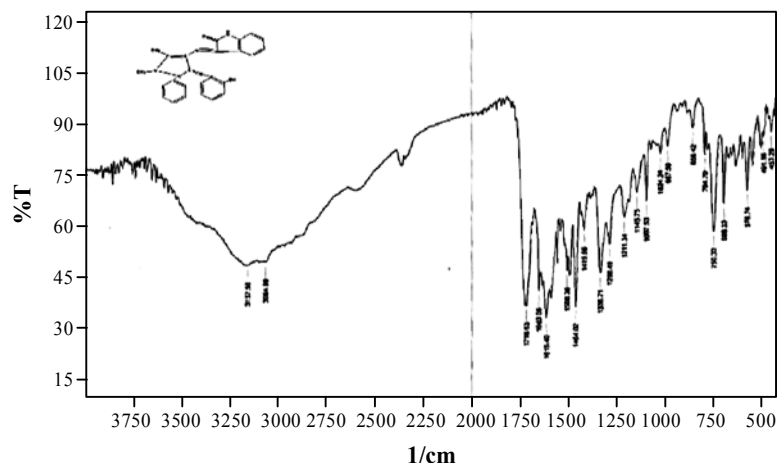
**Fig. 4: Experimental FTIR vibration spectra of 2-HDMIA**
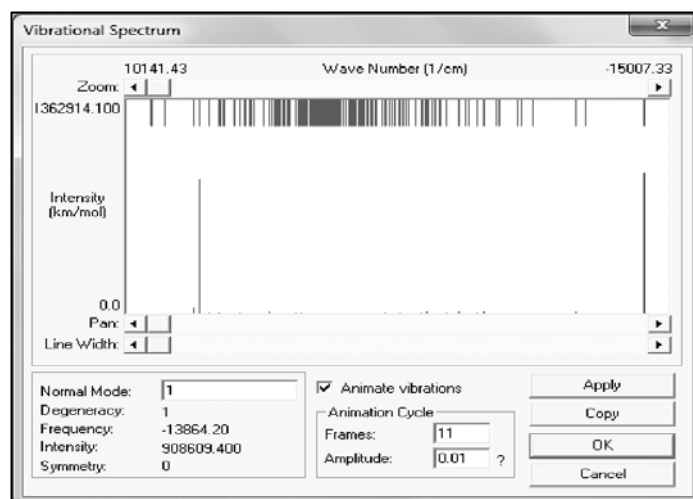
Fig. 5: Theoretical FTIR vibration spectra of 2-HDMIA

Electronic spectra

The electronic spectra of ligand (3-ADMIA) (Fig. 6) and (2-HDMIA) (Fig. 7) were studied and the spectral data were listed in Table 4. The UV-Vis spectrum of the Schiff base ligand (3-ADMIA) was characterized mainly by four absorption peaks at (278 and 345) nm assigned to ($\pi \rightarrow \pi^*$) and at (362 and 440) nm assigned to (n $\rightarrow \pi^*$). While the UV-Vis spectrum of the Schiff base ligand (2-HDMIA) was characterized mainly by two absorption peaks at (291) nm assigned to ($\pi \rightarrow \pi^*$) and at (460) nm assigned to (n $\rightarrow \pi^*$)[10].
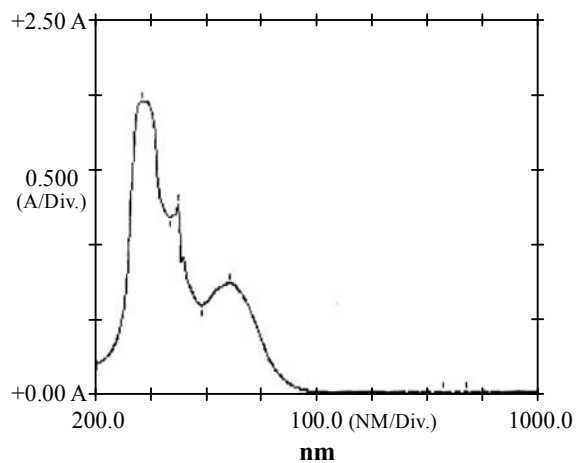
Fig. 6: Electronic spectra of (3-ADMIA)
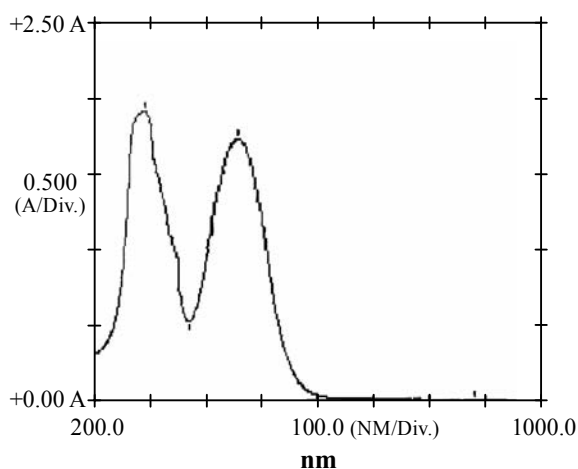
Fig. 7: Electronic spectra of (2-HDMIA)

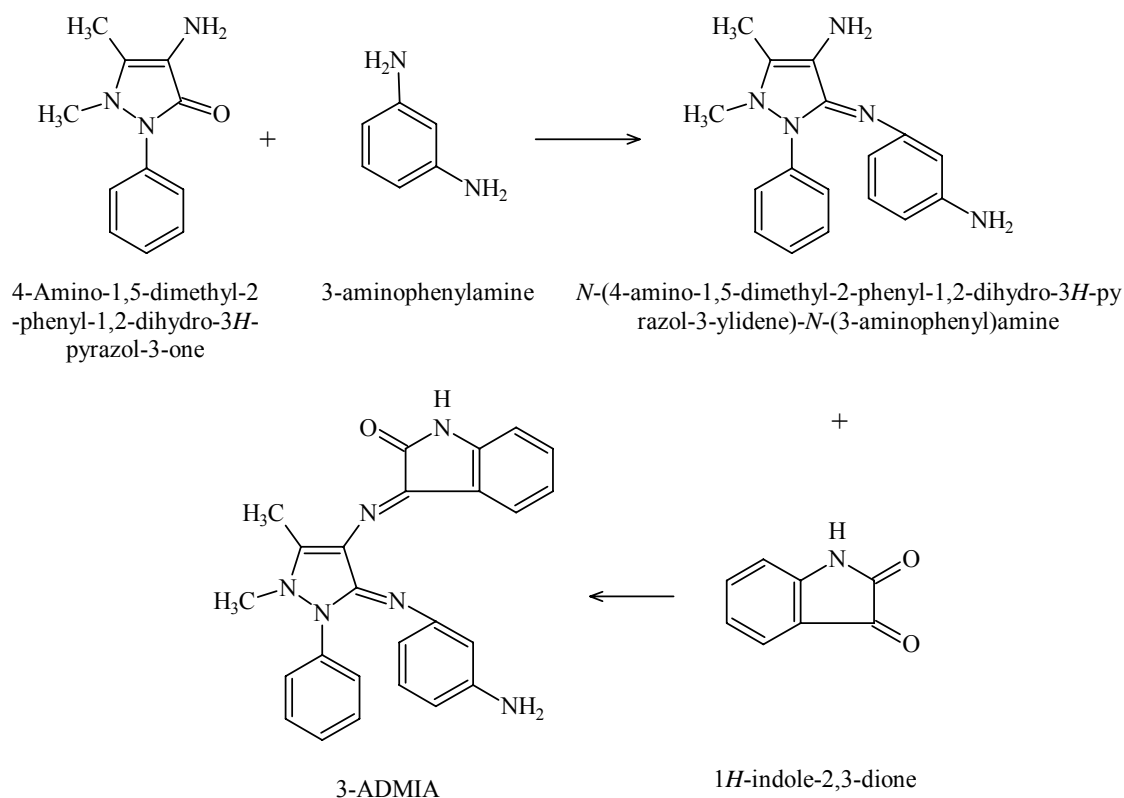**Table 4: Experimental UV/Visible spectra of synthetic compounds**

Compounds	λ_{max} (nm)	ν (cm^{-1})	ε_{max}	Transition
3-ADMIA	278	35971	1957	$\pi \rightarrow \pi^*$
	345	28986	1275	$\pi \rightarrow \pi^*$
	362	27624	888	$n \rightarrow \pi^*$
	440	22727	744	$n \rightarrow \pi^*$
2-HDMIA	291	34364	2317	$\pi \rightarrow \pi^*$
	460	21739	2141	$n \rightarrow \pi^*$

The chemical formula and physical properties of prepared compounds have been listed in Table 5.
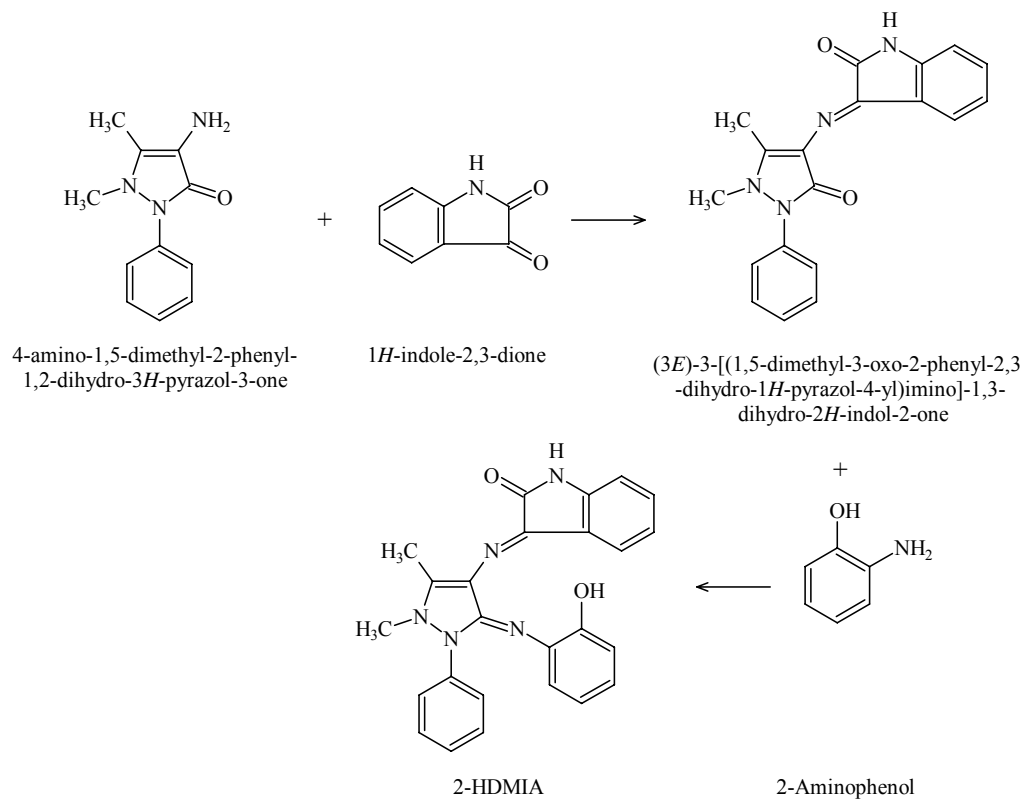
Table 5: The chemical formula and physical properties of prepared compounds

Compounds	Chemical formula	M. wt.	Yield (%)	Color	Melting point (°C)
3-ADMIA	$C_{25}H_{22}N_6O$	422.489	72	Brown	170
2-HDMIA	$C_{25}H_{21}N_5O_2$	423.474	69	Reddish-brown	168

Scheme 1 and 2, shows the diagrams of the consecutive reaction to synthesis different chemical compounds that may be useful as new Ligands in order to coordinate with different transition metals.

4-Amino-1,5-dimethyl-2-phenyl-1,2-dihydro-3*H*-pyrazol-3-one

3-aminophenylamine

N-(4-amino-1,5-dimethyl-2-phenyl-1,2-dihydro-3*H*-pyrazol-3-ylidene)-*N*-(3-aminophenyl)amine

3-ADMIA

1*H*-indole-2,3-dione

Scheme 1: Diagrammatic pathways of the synthesis reactions for the new Schiff base 3-ADMIA

4-amino-1,5-dimethyl-2-phenyl-
1,2-dihydro-3H-pyrazol-3-one

1H-indole-2,3-dione

(3E)-3-[(1,5-dimethyl-3-oxo-2-phenyl-2,3
-dihydro-1H-pyrazol-4-yl)imino]-1,3-
dihydro-2H-indol-2-one
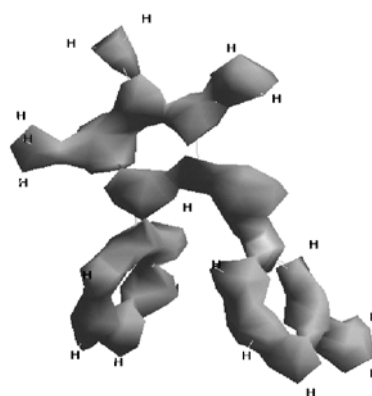

2-HDMIA

2-Aminophenol

**Scheme 2: Diagrammatic pathways of the synthesis reactions for the
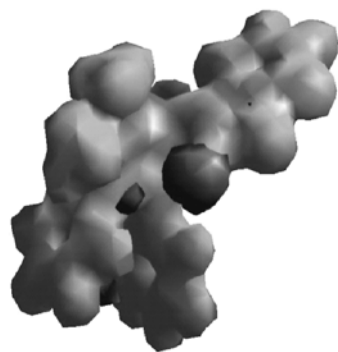new Schiff base 2-HDMIA**

Scheme 3 and 4, shows the physical and energy properties of Schiff bases compounds.
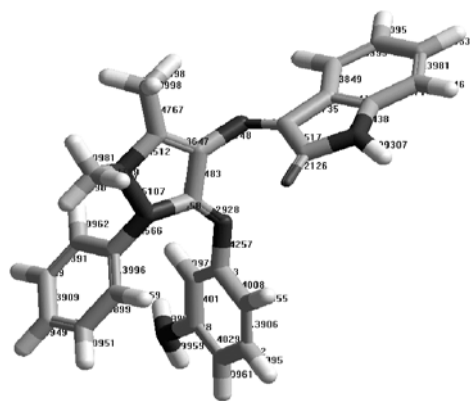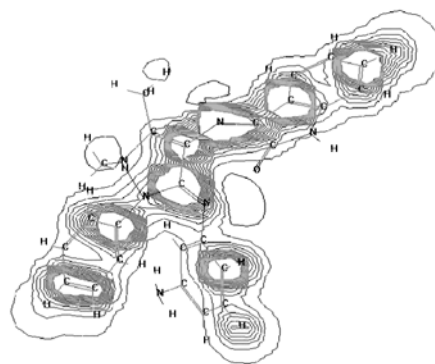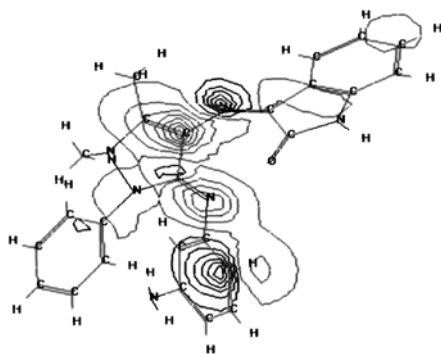

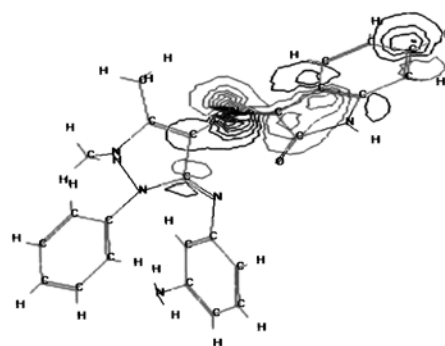**Long of bond with tube shape**

Total charge density (3D)

Electrostatic potential (3D)

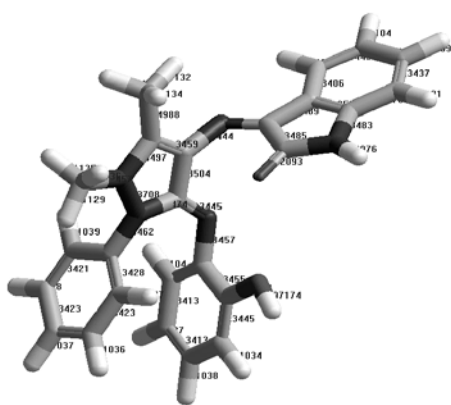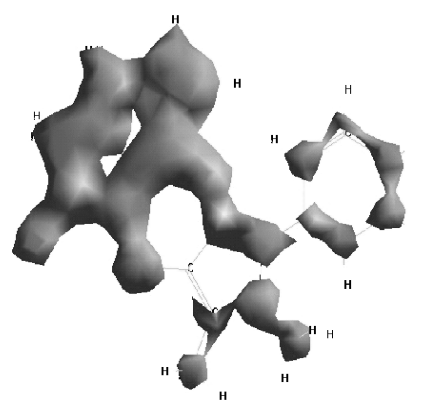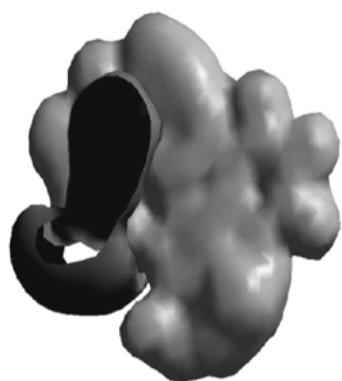**Electrostatic potential (2D)**

HOMO (2D)

LUMO (2D)

Scheme 3: Physical and energy properties of Schiff base 3-ADMIA

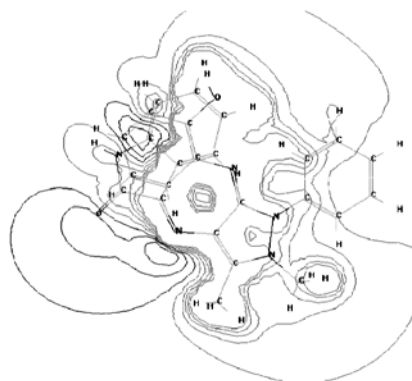
Long of bond with tube shape

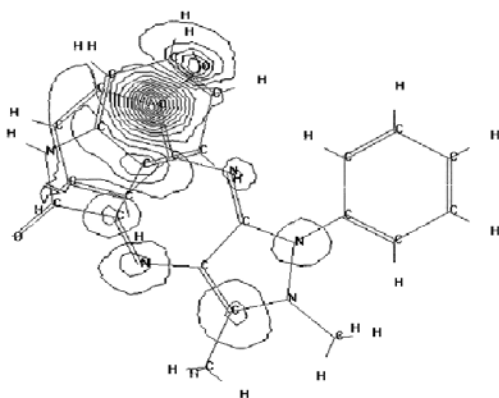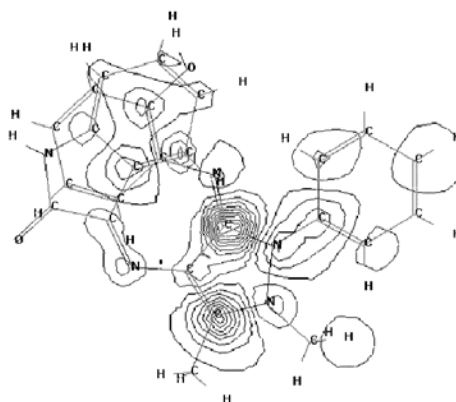

Total charge density (3D)

Electrostatic potential (3D)   **Electrostatic potential (2D)**

HOMO (2D)   **LUMO (2D)**

Scheme 4: Physical and energy properties of Schiff base 2-HDMIA

Application

New Schiff bases ligands can be synthesized according to the estimation study and performing through the comparative study between the experimental and theoretical results.

CONCLUSION

(i)   Second transition state is the most probable state to give up the reaction products than other transition states of 2- HDMIA.

    (ii)   First transition state is the most probable state to give up the reaction products than other transition states of 3-ADMIA.

    (iii)   They found a good agreement between the experimental and theoretical values of vibration spectrums of synthetic compounds.

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