

## THEORETICAL STUDY FOR COMPARISON OF pKa OF A NUMBER OF SCHIFF BASES BY EMPLOYING PARAMETERS DERIVED FROM DFT AND MP2 METHOD

Salah H.M. Sheet<sup>1</sup>, Rayan Basheer Mahmood<sup>1</sup>, Noor H.M. Saeed<sup>2\*</sup>  
Shakir Mahmood Saied<sup>3</sup>

<sup>1</sup>General Directorate of Education in Nineveh, Iraq

<sup>2</sup>Department of Chemistry, College of Education for Pure Science, University of Mosul, Mosul, Iraq

<sup>3</sup>College of Pharmacy, Al-Noor University, Mosul, Iraq

**Abstract.** The ionization constants of seven compounds derived from Schiff bases have been studied theoretically. In this study, the factors affecting the ionization constant pKa of Schiff bases were found, which are van der Waals forces, energy levels, hardness, chemical potential and spherical electrophile index by conducting a theoretical study of these compounds using two methods of quantum mechanics for the purpose comparison, which is the Ab-initio basic calculation methods. Two methods were chosen, which are the density function theory (DFT) method and the MP2 Mueller-Pleist perturbation theory method using Chem program. Office 2008 the extent to which these two methods correspond to the known chemical bases was determined by discussing the theoretical variables that were calculated using the two methods referred to above and finding the relationship between the calculated physical variables with each other and determining their nature.

After conducting the multiple statistical analysis process, it was found that the best variables that affect the ionization constant in the DFT method are (Bond C1-C7, Bend, VDW) and the rest of the variables were theoretically excluded because the coefficients of those variables are very few or equal to zero and accordingly these variables were adopted to obtain A relationship with better results, as it is noted that the values of the correlation coefficient in this DFT method are (0.994). As for the MP2 method, the best variables that affect the ionization constant are (I], KE, Tors) and the rest of the variables were theoretically excluded because the coefficients of these variables are very few or equal Therefore, these variables were adopted to obtain a relationship with better results, as it is noted that the values of the correlation coefficient in this MP2 method are (0.989).

By comparing the theoretical values with the practical values, it was found that the results of the DFT method were closer to the process than the results of the MP2 method.

**Keywords:** Schiff's rules, ionization constant, quantum mechanics, basic calculations, density function theory method, Mueller-Pleisette perturbation theory method.

**Corresponding Author:** Noor H.M. Saeed, Department of Chemistry, College of Education for Pure Science, University of Mosul, Mosul, Iraq, e-mail: [noorsaeed@uomosul.edu.iq](mailto:noorsaeed@uomosul.edu.iq)

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### 1. Introduction

Schiff's bases are compounds of great importance due to their many different applications in many fields and because of their physiological and biological activities

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(Hamed *et al.*, 2020; Yazici *et al.*, 2013). It was used in the field of industrial applications as corrosion inhibitors and in the manufacture of polymers and dyes (Naqvi *et al.*, 2009; Mohammed, 2011). It was also used as selective and sensitive reagents in determining minerals by forming colored complexes with a number of minerals (Tupare *et al.*, 2013) and it was also used in the field of medicine and pharmacy where it was used as antibiotics. In addition, it has been used in the field of biological application (Kumar, 2010; Da Silva *et al.*, 2011).

Schiff's bases gained great importance, especially in the field of pharmacology and pharmaceutical compounds (Pranker, 2007), due to the presence of imine groups (C=N) in their structure and the ease of their preparation from a wide range of substituted amines and aromatic aldehydes. For this reason Schiff's rules gained great activities and became of great importance in such kind of applications, which stimulated many researchers and encouraged them to work in such field (Da Silva *et al.*, 2011; Geremia & Seybold, 2019).

The value of the acid dissociation constant (pKa) is an important chemical function that helps determine the chemical behavior of many types of compounds such as Schiff bases (Butcher *et al.*, 2015). They estimate the ionization ratio of these compounds in the aqueous solution that produces the hydronium ion and the conjugate base of the separated compound. One of the most important applications of this function is to determine the stability of the drug, its distribution in the body and its absorption (O'Donnell, 2019).

This function can also be used as a measure of acid strength. Mathematically, the pKa value is equal to the negative value of the logarithm of the acid ionization constant (Ka). The low value of pKa indicates the strength of the acid and the farthest extent of the acid's dissociation in water. In this case, the acidity is related to the stability of the conjugate base resulting from the ionization process, which in turn depends on its ability to rotate the new pair of electrons in its structure due to ionization. Therefore, the pKa value is affected by electronic factors (inductive and electrical) represented by electrons that donate or withdraw substitutions. The presence of a group (C = N imine) in the structure of the Schiff base makes the aromatic ring rotate to reduce the stress that can arise as a result of the replacement of spatially adjacent large molecules on the rings. The pKa values are sensitive to the change in the electronic effects as well as the geometry resulting from the spatial distribution of the molecule. This factor can be estimated by quantitative mechanical methods (Da Silva *et al.*, 2011; Schilling & Luber, 2019). In terms of variables such as electronic density and charges, total energy of the molecule, energies of molecular orbitals HOMO and LUMO and other variables will be mentioned later in this research (Sadeek *et al.*, 2023), although there are many practical methods used to estimate pKa values, but they are all unable to provide the effects of these factors are quantified.

This case gives preference to theoretical methods and it obviates the need for laboratory equipment and chemicals in their absence. In this research, two methods were used, namely DFT and mp2 from quantum mechanics methods, which are one of the basic ab initio methods, to choose the ability of these two methods to evaluate the pKa values of the Schiff rule chosen for this study and to predict the pKa value of the compounds of the related structures without the need for work (Ali *et al.*, 2023; Ramachandran *et al.*, 2008).

The value of pKa has become one of the most common physical and chemical functions (Saleh *et al.*, 2022; Thapa & Schegel, 2015) because of its relationship to the concept of the pH function. Many experimental methods have been used to determine

pKa values (Reijenga *et al.*, 2013) and its calculation is important to many researchers in this field.

### **Computational chemistry**

Computational chemistry is a branch of advanced, modern and distinguished chemistry at the present time. Its aim is to find the most important characteristics of a chemical compound and compare them with the values measured by practical methods. Computational chemistry (Gramer, 2004; Atkins & Paula, 2011) includes different mathematical methods, which fall into two main categories:

1. Molecular Mechanics, depends mainly on the use of Newton's laws and its application to atoms without taking into account the influence of electrons (Cramer, 2002).

2. Quantum Mechanics, which mainly includes the Schrodinger equation to describe particles, taking into account the presence and influence of electrons. Quantum mechanics methods are divided into two types: Ab-initio and Semi-empirical.

In this research, we will discuss the Ab initio Methods of basic calculations, that Ab initio means basic calculations or calculations from the beginning (Bargon, 2004) and it includes a mathematical solution for all arithmetic integrals and thus it faces difficulties resulting from the large number of integrals that require its calculation and from the basic calculation methods that will Two methods are used in this research, the first is the density function theory (DFT) method (Density Functional Theory), this theory was used for the first time and developed later by researchers Hohenberg-Kohn in 1964 AD and it later became one of the methods of fundamental analyzes, which was used extensively in theoretical studies Especially after the development in the field of electronic accounts (Parr & Yang, 1989).

This theory is based on finding the electronic properties of the molecule in the steady state, which are found using the electronic density. The advantage of this theory is that it includes finding approximate electronic correlations with greater accuracy than extracted using the (HF) method and this means that the density function theory is of such quality that it can be used with acceptable confidence in theoretical studies (Hamdoon *et al.*, 2022).

Perturbation theory (MP2) whose main idea was published as early as 1934 by Christian Müller and Milton S. Plesset theory is a widely used method for approximating the binding energy of molecules. In particular, the Møller-Plesset perturbation theory of second order (MP2) is one of the simplest and most useful levels of theory after the Hartree-Fock approximation (Lee & Head-Gordon, 2018).

### **Relational analysis in chemistry**

Correlational analysis includes finding the relationship and correlation between two or more variables, as it is of great benefit in computational chemistry. Correlational analysis generally depends on finding the relationship between two sets of data, one of which represents research results obtained experimentally and the other represents data from previous studies found in the literature or data It has been calculated theoretically and the relationship is established by drawing the obtained data (which can be termed as a dependent variable (Y) against the previously calculated data (which is named as an independent variable (X) Independent Variable) and often Relationships of this type are linear and give straight lines with a section (b) on the vertical axis and an inclination (a),

which reflects the sensitivity of the dependent variable towards changes in the future (Saleh *et al.*, 2023).

The straight line equation can be written as follows:

$$Y = ax + b \quad (1)$$

And you can infer that the relationship between the variables (Y, X) applies to the straight line equation only when the dispersion of points around the straight line is within the experimental error. On the other hand, if the dispersion of points around the straight line is outside the acceptable error range, this indicates that the relationship between The two variables (Y, X) are not a linear relationship, that one variable is not sufficient to clarify the experimental results and it is often necessary to use more than one variable in the correlational analysis to clarify or describe a particular system.

In this case, we will talk about a type of regression analysis called Multiple Parametric Regression Analysis. The multivariate linear regression equation can be written for a dependent variable (Y) with a series of independent variables ( $X_1, X_2, X_3, \dots$  etc) as in the following figure:

$$Y = a_0 + a_1x_1 + a_2x_2 + a_3x_3 + a_4x_4 \quad (2)$$

Since ( $a_0$ ) is the measurement coefficient that gives the value (Y) to a reference case and the regression coefficients ( $a_1, a_2, a_3 \dots$  etc) are of standard statistical importance, as they describe the percentage of (y) susceptibility to change against the variable concerned and the degree of success of the correlation in This case can be estimated through the values of standard deviation and correlation coefficient (Shorter, 1973).

### **The practical part (theoretical calculations)**

Theoretical calculations include the selection of seven compounds from Schiff bases whose formulas and pKa ionization constants are shown in Table 1 (Saleh *et al.*, 2022), which were studied by calculating some physical variables for the compounds using chemical programs of the type Chem. Office 2008 and Gaussian.

Among the information that can be obtained by using the molecular mechanics method (Shorter, 1973) included in the program (MM2) (Molecular Mechanic) is the completion of the energy reduction process to obtain the most stable form (the least energy) and the conduct of energy calculations to compare between two bodies of the same molecule and the steric bodies that it occupies molecules by determining the angle confined between the plane of the dihedral angle) and studying the molecular motion using molecular dynamics.

As for the information that can be obtained from quantum mechanics methods and by using the Gaussian sub-program within the Chem program. Office, they are many, including (Saied *et al.*, 2022) the energy of molecular orbitals (HOMO - LUMO) and the heat of formation (Heat of formation) to evaluate the energies of stability of different molecule structures and molecular atomic charges calculated from the coefficients of molecular orbitals, voltage or electrostatic energy and dipole moment and the bodies and energies of transition states, the energy of bond dissociation.

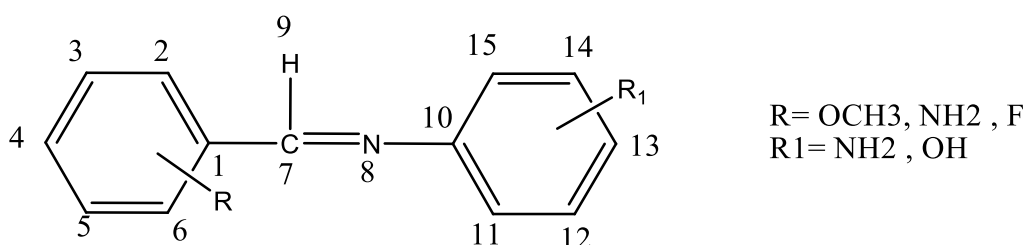
Then the statistical analysis was conducted between the selected variables calculated theoretically with the values of the ionization constant pKa obtained from the literature and the values of the correlation coefficient were adopted as a measure for this purpose and to find out the extent of the relationship between the values of the ionization constants of the Schiff rules shown in Tables 3, 4 and between the values of the energy functions HOMO, LUMO, hardness, chemical potential and electrophilic index....etc that

were calculated according to Schiff's rules using the DFT method and the MP2 method, as it is possible to know the effect of these variables and the strength of their correlation to find pKa values through R2 values, because they represent a measure of the strength of the relationship (Muraleedharan, 2017; Caballero-García *et al.*, 2018).

R2 values were found by performing a simple linear regression analysis using (Statistical Program of Science Society SPSS 2018).

## 2. Results and discussion

Theoretically, some physical constants of Schiff's rules were calculated, such as steric energy and Millikan charge, as well as calculating higher occupied orbital energy HOMO, lower unoccupied orbital energy LUMO, hardness  $\eta$ , chemical electron potential  $\mu$  and general electrophilic index  $W$ , in order to Linking it to the ionization constant pKa and finding out the extent of its impact by conducting the statistical analysis process. Table 1 shows the structural formulas of Schiff's rules.



**Figure 1.** Composition and numbering of atoms for the selected compounds listed in Table 1

Total energy values were calculated using the program (Molecular Mechanics (MM2)), while the rest of the physical constants (charges, HOMO, LUOM,  $\eta$ ,  $\mu$ ,  $W$ ) were calculated using the basic calculation methods Abinitio method (MP2), (DFT / B3LYP) and choosing These two methods were based on being the most common and most widely used in this field of studies, then the values of the physical constants theoretically calculated by the DFT and (MP2) method were linked with the practical values of the ionization constants pKa and then deduced mathematical equations through which the ionization constants for unknown compounds are calculated It is difficult to measure practically.

**Table 1.** Names, structural formulas and values of ionization constants for compounds of Schiff bases

No.	Compound	Structure	pKa
1	R=4-OH, R <sub>1</sub> =13-NH <sub>2</sub>		5.5703
2	R=4-OCH <sub>3</sub> , R <sub>1</sub> =13-NH <sub>2</sub>		12.0071

3	R=6-NH <sub>2</sub> , R <sub>1</sub> =12-OH		5.0654
4	R=6-NH <sub>2</sub> , R <sub>1</sub> =13-OH		6.4392
5	R=6-F , R <sub>1</sub> =11-OH		10.8390
6	R=6-F , R <sub>1</sub> =12-OH		12.0386
7	R=6-F , R <sub>1</sub> =13-OH		11.0559

### Spatial arrangement effect

What is meant by the spatial arrangement is the geometric shape that can be taken by the compounds of the Schiff bases and the distribution of atoms in the vacuum, which is controlled by various factors: the first is the obstruction factor, which works to increase the push of electrons for the obstructed atoms in the far direction to mitigate the repulsion caused by these groups, the second effect is Different spatial interactions such as van der Waals forces and hydrogen bonds. This force as a whole can work together or oppose one another and the outcome of these overlaps can increase or decrease the stability of the molecule, depending on its value. Based on the foregoing, some theoretical variables were chosen such as Stretch, Bend, Stretch-Bend, Torsion, Non-1,4VDW and the energy of Van der Waals interferences of the type 1,4VDW, Total energy. It was calculated as a model to describe the effect of the active sites on the reaction centers in the compounds

of Schiff bases under study (Saleh *et al.*, 2024). The values of these variables calculated theoretically by the MM2 method were included in Table 2.

**Table 2.** The theoretically calculated values of the variables using the MM2 method

Comp.	PKa	strech	Bend	Stretch Bend	Torsion	Non-1,4VDW	VDW 1,4	Total energy	Dipole dipole
1	5.5703	0.4553	3.0158	0.0839	-15.4469	-0.7008	6.3484	-6.2266	0.0179
2	12.0071	0.7145	4.5746	0.1567	-15.4447	0.1658	10.2135	0.4939	0.1135
3	5.0654	0.5264	3.0948	0.0956	-13.3290	-0.4202	6.3641	-3.5494	0.1190
4	6.4392	0.5043	3.1059	0.0951	-13.3305	-0.4844	6.3862	-3.6464	0.0772
5	10.8390	0.5412	3.0914	0.0440	-12.2546	-0.2259	7.1733	-0.8610	0.7697
6	12.0386	0.4432	2.9839	0.0665	-12.2728	-0.2040	7.1736	-1.7594	0.0501
7	11.0559	0.4797	2.9396	0.0780	-12.2662	-0.2009	7.1274	-1.8344	0.0080

It is noted from the table that the value of the total steric obstruction energy varies in the compounds and that most of the values that control these energies depend mainly on the values of each of the 1.4 VDW correlational van der Waals interferences resulting from the increase in the ring size and range between (6.3484-10.2135 Kcal/ mol) and the values of The non-correlation van der Waals interferences that range between {0.1658-(-0.7008)Kcal/mol} and the stretch-bend values are highest in the second compound (0.1567) and the lowest in compound No. (5), where its value is (0.0440), while the effect of Stretch, bend energy and quadrilateral torsion are close (Majihool *et al.*, 2023).

### Theoretical calculations of energy functions

The HOMO and LUMO orbital energy values for the compounds under study were calculated using the DFT method and the MP2 method and then the orbital energies were used to calculate some functions known in the literature (Owaid *et al.*, 2022) that are related to the stability of molecules and their interactive tendency in terms of being electrophilic or nucleophile and among these functions is the hardness of the molecule (Hardness ( $\eta$ )), Electronic Chemical Potential ( $\mu$ ) and Global Electrophilicity Index (W) which were calculated from special equations.

Two types of Molecan atomic charges, low charges and kinetic energy were determined and the results were included in Tables 3 and 4.

**Table 3.** The values of energy variables calculated theoretically for compounds of Schiff bases using DFT (3.21G) method

Comp. No.	PKa	H	L	$\eta$	$\mu$	W	Bond C1-C7
1	5.5703	-0.1821	-0.0388	0.07165	-0.11045	-0.0855130	1.054
2	12.0071	-0.1752	-0.0273	0.07395	-0.10125	-0.069314	1.044
3	5.0654	-0.1891	-0.0417	0.07135	-0.1154	-0.0933227	1.058
4	6.4392	-0.1844	-0.0377	0.07335	-0.11105	-0.0840634	1.055
5	10.8390	-0.2064	-0.0560	0.0752	-0.1312	-0.1144510	1.034
6	12.0386	-0.2117	-0.0572	0.07725	-0.2689	-0.4680078	1.025
7	11.0559	-0.2067	-0.0500	0.07835	-0.12835	-0.1051290	1.027
Comp. No.	PKa	Bond C7N8	Bond N8C10	LC-N8	MC-N8	TE x 10 <sup>-3</sup>	KT x 10 <sup>-3</sup>
1	5.5703	1.637	0.966	0.151649-	-0.613534	-428.666	425.270
2	12.0071	1.652	0.973	0.151245-	-0.611319	-453.181	449.522
3	5.0654	1.645	0.965	0.158484-	-0.610860	-428.662	425.268

4	6.4392	1.645	0.976	0.157417-	-0.612310	-428.663	425.277
5	10.8390	1.647	0.980	0.134536-	-0.594862	-456.054	452.475
6	12.0386	1.638	0.941	0.144168-	-0.604267	-456.055	452.495
7	11.0559	1.658	0.970	0.141270-	-0.598395	-456.056	452.506

**Table 4.** The values of energy variables calculated theoretically for compounds of Schiff bases using MP2 (3.21G) method

Comp. No.	PKa	H	L	$\eta$	$\mu$	W	Bond C1-C7
1	5.5703	-0.2534	0.0871	0.17025	-0.08315	-0.0203052	0.977
2	12.0071	-0.2525	0.0879	0.1702	-0.0823	-0.019898	0.979
3	5.0654	-0.2773	0.0723	0.1748	-0.1025	-0.0300522	0.987
4	6.4392	-0.2691	0.0775	0.1733	-0.0958	-0.0264790	0.988
5	10.8390	-0.2895	0.0643	0.1769	-0.1126	-0.035835	0.962
6	12.0386	-0.2890	0.0608	0.1749	-0.1141	-0.0372178	0.961
7	11.0559	-0.2870	0.0678	0.1774	-0.1096	-0.033856	0.963
Comp. No.	PKa	Bond C7N8	Bond N8C10	LC-N8	MC-N8	TE x 10 <sup>-3</sup>	KT x 10 <sup>-3</sup>
1	5.5703	1.564	0.893	-0.13990	-0.557261	-427.1235169	425.9980474
2	12.0071	1.563	0.893	-0.139984	-0.559402	-451.536096	450.3013644
3	5.0654	1.562	0.885	-0.134437	-0.543802	-427.1202095	425.9991123
4	6.4392	1.558	0.894	-0.137490	-0.548370	-427.1207113	425.9885222
5	10.8390	1.569	0.906	-0.119735	-0.527643	-454.4876274	453.220215
6	12.0386	1.575	0.880	-0.128805	-0.541398	-454.4897417	453.2311356
7	11.0559	1.570	0.891	-0.132198	-0.547009	-454.4902527	453.2275107

The main purpose of calculating these variables is to use them in the regression analysis to reach the most important variables affecting the values of the ionization constants pKa and accordingly, these calculations were followed with statistical treatment for the purpose of evaluating the relationship between each of these calculated functions and the nature of their impact on the values of the ionization constants pKa as a dependent factor and before evaluating the variables and to test its validity and accuracy, it was necessary to know the relationship between the unreliable functions with each other, which enables us to estimate these effects with each other and then choose the variables used in the statistical analysis on sound scientific and statistical bases (Al-Thakafy *et al.*, 2024).

The relationship between each of the variables with each other was found using the DFT method and the MP2 method used for the compounds of Schiff bases using the single and multiple regression analysis process, as well as the values of the ionization constant pKa, and the results were included in Tables 5 and 6.

The tables 5 and 6 showed that there is a good relationship between some variables and the ionization constant pKa and these relationships vary in their values according to the method used. This study showed a clear correlation between the values of some of the calculated variables, which encouraged us to continue and move to the next stage, which included conducting the binary and triple regression analysis process for the purpose of reaching the relationships final.



**Table 5:** The values of the correlation coefficient (R2) for the relationship between the theoretically calculated physical variables using the DFT method and the ionization constants pKa

Var	pKa	HOMO	LUMO	$\eta$	$\mu$	W	LC-N <sub>8</sub>	MC-N <sub>8</sub>	TE	KE	BondC <sub>1</sub> -C <sub>7</sub>	BondC <sub>1</sub> -N <sub>8</sub>	BondN <sub>8</sub> -C <sub>10</sub>	Str.	Bend	Str.-Bend	Torsion	Non1,4VDW
pKa	1																	
HOMO	0.232	1																
LUMO	0.108	0.941	1															
$\eta$	0.663	0.594	0.377	1														
$\mu$	0.209	0.479	0.453	0.307	1													
W	0.190	0.401	0.381	0.257	0.994	1												
LC-N <sub>8</sub>	0.507	0.558	0.514	0.526	0.117	0.081	1											
MC-N <sub>8</sub>	0.378	0.705	0.622	0.557	0.085	0.049	0.852	1										
TE	0.948	0.368	0.218	0.711	0.196	0.166	0.680	0.578	1									
KE	0.636	0.110	0.015	0.582	0.237	0.233	0.108	0.072	0.546	1								
BondC <sub>1</sub> -C <sub>7</sub>	0.762	0.665	0.482	0.907	0.417	0.361	0.707	0.635	0.847	0.542	1							
BondC <sub>1</sub> -N <sub>8</sub>	0.170	0.003	0.019	0.191	0.177	0.209	0.062	0.169	0.201	0.167	0.083	1						
BondN <sub>8</sub> -C <sub>10</sub>	0.031	0.159	0.146	0.074	0.761	0.797	0.001	0.008	0.021	0.217	0.127	0.272	1					
Str.	0.099	0.307	0.415	0.035	0.214	0.189	0.015	0.027	0.051	0.027	0.027	0.222	0.212	1				
Bend	0.133	0.369	0.502	0.024	0.102	0.076	0.034	0.098	0.053	0.103	0.015	0.110	0.062	0.897	1			
Str.-Bend	0.0	0.633	0.820	0.111	0.178	0.134	0.353	0.425	0.022	0.066	0.162	0.081	0.025	0.584	0.741	1		
Torsion	0.094	0.802	0.738	0.427	0.262	0.204	0.281	0.582	0.177	0.023	0.366	0.034	0.036	0.226	0.380	0.524	1	
Non1,4VDW	0.704	0.009	0.007	0.247	0.017	0.017	0.120	0.110	0.609	0.499	0.274	0.351	0.001	0.523	0.513	0.190	0.004	1
1,4VDW	0.438	0.095	0.203	0.034	0.010	0.006	0.016	0.0	0.305	0.331	0.055	0.195	0.016	0.759	0.875	0.492	0.159	0.782

**Table 6:** The values of the correlation coefficient (R2) for the relationship between the theoretically calculated physical variables using the MP2 method and the ionization constants pKa

Var	pKa	HOMO	LUMO	$\eta$	$\mu$	W	LC-N <sub>8</sub>	MC-N <sub>8</sub>	TE	KE	BondC <sub>1</sub> -C <sub>7</sub>	BondC <sub>1</sub> -N <sub>8</sub>	BondN <sub>8</sub> -C <sub>10</sub>	Str.	Bend	Str.-Bend	Torsion	Non1,4VDW	VDW
pKa	1																		
HOMO	0.122	1																	
LUMO	0.141	0.975	1																
$\eta$	0.076	0.914	0.804	1															
$\mu$	0.130	0.996	0.991	0.875	1														
W	0.151	0.987	0.997	0.842	0.995	1													
LC-N <sub>8</sub>	0.184	0.713	0.708	0.627	0.715	0.727	1												
MC-N <sub>8</sub>	0.043	0.736	0.722	0.665	0.735	0.730	0.919	1											
TE	0.948	0.235	0.244	0.190	0.240	0.264	0.326	0.122	1										
KE	0.948	0.235	0.244	0.189	0.240	0.263	0.326	0.122	1.000	1									
BondC <sub>1</sub> -C <sub>7</sub>	0.557	0.399	0.423	0.307	0.411	0.445	0.498	0.250	0.706	0.706	1								
BondC <sub>1</sub> -N <sub>8</sub>	0.476	0.431	0.502	0.266	0.462	0.505	0.397	0.203	0.594	0.594	0.882	1							
BondN <sub>8</sub> -C <sub>10</sub>	0.004	0.004	0.021	0.007	0.009	0.012	0.119	0.093	0.014	0.014	0.010	0.051	1						
Str.	0.099	0.215	0.236	0.154	0.224	0.223	0.054	0.089	0.050	0.050	0.080	0.130	0.088	1					
Bend	0.133	0.362	0.347	0.341	0.358	0.343	0.163	0.259	0.052	0.052	0.067	0.084	0.013	0.897	1				
Str.-Bend	0.0	0.563	0.564	0.489	0.567	0.569	0.602	0.632	0.022	0.022	0.343	0.289	0.036	0.584	0.741	1			
Torsion	0.094	0.966	0.927	0.907	0.956	0.938	0.622	0.688	0.178	0.178	0.302	0.310	0.002	0.226	0.38	0.524	1		
Non1,4VDW	0.704	0.010	0.011	0.007	0.010	0.013	0.028	0.0	0.608	0.608	0.104	0.090	0.001	0.523	0.513	0.190	0.004	1	
1,4VDW	0.438	0.131	0.120	0.134	0.128	0.114	0.033	0.128	0.303	0.303	0.007	0.002	0.010	0.759	0.875	0.492	0.159	0.782	1

Through multiple statistical analysis, it was found that the best variables that affect the ionization constant in the DFT method are (Bond C1-C7, Bend, VDW) and the rest of the variables were theoretically excluded because the coefficients of those variables are very few or equal to zero and accordingly these variables were adopted to obtain a relationship With better results, as it is noted that the values of the correlation coefficient in this DFT method are (0.994), but in the MP2 method, the best variables that affect the ionization constant are ( $\eta$ , KE, Tors) and the rest of the variables were theoretically excluded because the coefficients of those variables are very few or equal to zero and accordingly These variables were adopted to obtain a relationship with better results, as it is noted that the values of the correlation coefficient in this MP2 method are (0.989) and the results were included in Table 7.

**Table 7.** Results of multiple regression analysis. Correlation between selected physical variables and ionization constants pKa

Method	Var	Const. B	Parameter X <sub>1</sub>	Parameter X <sub>2</sub>	Parameter X <sub>3</sub>	R <sup>2</sup>	SE
DFT	pKa&BondC1-C7 Bend VDW	402.919	-386.854	14.041	-5.016	0.994	0.345
MP2	pKa& $\eta$ , KE, Tors	21.721	-596.653	-0.232	0.853	0.989	0.477

After conducting the multiple regression analysis process, it was found that the best variables that affect the ionization constants of the Schiff bases compounds using the DFT method are Bond C1-C7, the bending energy, the VDW interconnections, and the MP2 method are  $\eta$ , KE, Tors, and the rest of the variables were excluded theoretically because the coefficients of these variables It was little or equal to zero, and therefore these three variables were adopted only to obtain a mathematical relationship through which the ionization constant can be calculated for a number of Schiff's rules, which are difficult to calculate the ionization constant accurately in practice (Hussein *et al.*, 2022).

Based on these results, the mathematical relationship listed below (Equation 3 and 4) was established to calculate the values of the ionization constant for a number of Schiff's rules and compare them with the practical values whose results are listed in Tables 8 and 9.

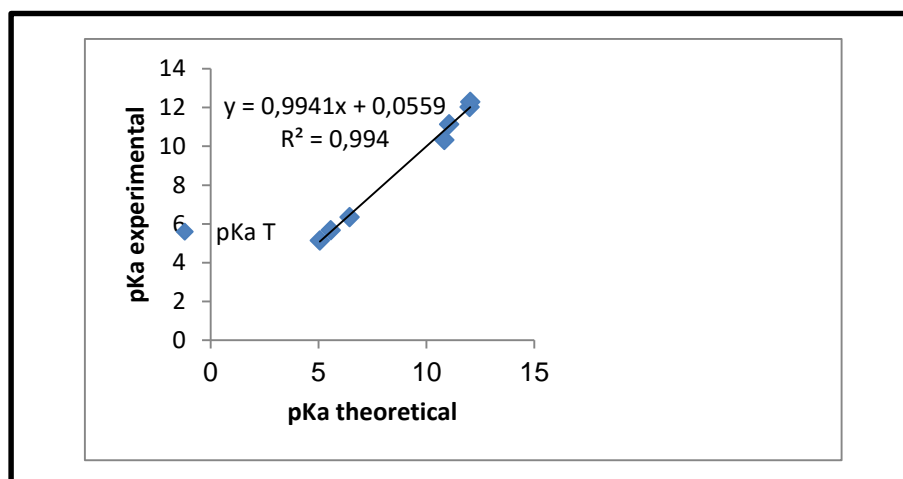
$$Y = 402.919 - 386.854 * \text{Bond C1} - \text{C7} + 14.041 * \text{Bend} - 5.016 * \text{VDW} \quad (3)$$

$$Y = 21.721 - 596.653 * \eta - 0.232 * \text{TE} + 0.853 * \text{Tors} \quad (4)$$

Tables 8 and 9 show that the value of the correlation coefficient resulting from drawing the relationship between the practical and theoretical values of the ionization constant was close to (0.944) for the DFT method.

**Table 8.** Schiff bases ionization constant values by the experimental and theoretical DFT method

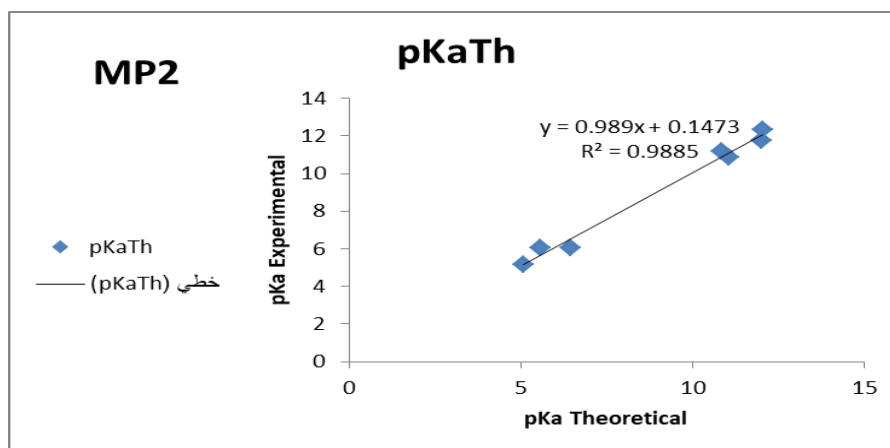
Comp.	pKa <sub>exp</sub>	pKa <sub>thio</sub>	$\Delta$ pKa
1	5.5703	5.676157	-0.105857
2	12.0071	12.04447	-0.03737
3	5.0654	5.159229	-0.093829
4	6.4392	6.364793	0.074407
5	10.839	10.33704	0.50196
6	12.0386	12.30781	-0.26921
7	11.0559	11.14383	-0.08793



**Figure 2.** The graphical relationship between the ionization constant of Schiff's rules and the theoretically calculated method

**Table 9.** Schiff bases ionization constant values in the practical and theoretical MP2 method

Comp.	pKa <sub>exp</sub>	pKa <sub>thio</sub>	ΔpKa
1	5.5703	6.0572	-0.4869
2	12.0071	11.75268	0.25442
3	5.0654	5.148305	-0.082905
4	6.4392	6.042121	0.397079
5	10.839	11.16089	-0.32189
6	12.0386	12.33914	-0.30054
7	11.0559	10.85314	0.20276



**Figure 3.** The graphical relationship between the ionization constant of Schiff's rules and the theoretically calculated by MP2 method

### 3. Conclusions

1. The possibilities of using quantum mechanics methods in our study, which were represented by basic calculations - the DFT method and the MP2 method. Which were used to calculate the ionization constant values of the Schiff rules.

2. The DFT method gave accurate results and is in agreement with the previous experimental study better than the MP2 method.

3. There are very strong relationships for the selected variables BondC1-C7, Bend and VDW in calculating the ionization constant values for the Schiff bases under study.

4. There is a convergence between the practical values in the previous study with the theoretical values obtained in this study using the DFT method and this indicates the accuracy of the variables that were chosen in the theoretical calculations.

#### Recommendations

1. Applying the DFT method to other Schiff base compounds for other practical studies and comparing the results.

2. Extensive study of the ionization constant for some variables using the DFT method and comparing them with other practical studies and knowing the extent to which the theoretical results match the studied practical results.

3. A practical study of Schiff's rules with other groups such as (methyl, phenol, pyridine, aniline) and other compensators at ortho, para and meta sites and calculating their ionization constant and comparing them with theoretical values.

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