

Theoretical study of structure and vibrational frequencies of pyrazole and its derivatives, and x-ray structure determination

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Abstract

Five compounds have been prepared and studied; Pyrazole, 3,5-dimethylpyrazole , 3,5-dimethyl -1 N phenyl pyrazole, 3,5-diphenylpyrazole and p-toluene sulfonyl pyrazole . Molecular orbital calculations using ab initio method / MP₂ theory at 6-31G(d,p) basis set were performed to determine the geometrical parameters, bond lengths and bond angles , were compared with x-ray analysis results. X-ray measurements showed that pyrazole exists as tautomeric mixture in the solid state , other physical properties such as total energy, dipole moments , charges on the atoms were also determined and discussed . The vibration frequencies were theoretically calculated at the same theory level for optimization and experimentally measured. Key words : Ab initio calculations , structure , vibrational frequencies, x-ray structural

determination , pyrazole and its derivatives

ملخص

حضرت و درست خمسة مركبات هي البايразول و 3,5- ثنائي ميثيل بايرازول و 3,5- ثنائي ميثيل N-1 فنيل بايرازول و 3,5- ثنائي فنيل بايرازول و بارا- تلوين سلفونيل بايرازول . وأجريت لها حسابات الأوربيتالات الجزيئية باستخدام طريقة ab initio عند المستوى النظري MP2 والمجموعة الأساسية 6-31G(d,p) لتعيين المعاملات الهندسية وأطوال الأواصر والزوايا ومقارنتها بنتائج تحليل الحيود الأشعة السينية وقد أظهرت قياسات الأشعة السينية أن البايразول يوجد بشكل خليط توتوميري في الحالة الصلبة . وكذلك تم حساب بعض الخصائص الفيزيائية للمركبات مثل الطاقة الكلية وعزم ثنائي القطب والشحن على الذرات ومناقشتها على أساس التركيب . وتم حساب الترددات التذبذبية نظريا وعند نفس المستوى للموائمة الهندسية ومقارنتها بأطياف تحت الحمراء المقاسة .

كلمات المفتاح: حسابات ab initio والتراكيب والترددات التذبذبية وتعيين التراكيب بواسطة حيود الأشعة السينية , بايرازول ومشتقاته

1.Introduction

Pyrazole is an aromatic heterocyclic compound containing two bonded nitrogen atoms. It is related to many compounds such as isoxazole, isothiazole, oxazole and imidazole⁽¹⁾. Pyrazole and its derivatives have widespread applications in the field of medicine and industry. They are used as antihypertensives⁽²⁾, anti thrombotic⁽³⁾, anti inflammatory⁽⁴⁾, anti microbial⁽⁵⁾, anti rheumatic⁽⁶⁾, anti tumor⁽⁷⁾, anti viral⁽⁸⁾ and anti diabetic⁽⁹⁾. Some derivatives are used as anti corrosion and for coloured photography. Pyrazole molecule is stabilized by resonance structure⁽¹⁰⁾ and possesses amphoteric probability⁽¹¹⁾. However it undergoes cyclic tautomerism in solution by exchange of the proton between the two atoms of the aromatic ring⁽¹²⁾. On the other hand, it undergoes electrophilic substitution at 4-position and the two positions 3 and five are equivalent. Since the nitration halogenations and acylation occur at 4-position^(13,14). The aim of the present work was devoted to investigate theoretically the structure and vibrational frequencies of pyrazole and substituted pyrazoles and compare it with x-ray structural analysis and IR measurements.

2. Experimental

2.1. Preparations

The studied compounds, pyrazole(S₁), 3,5-dimethyl pyrazole(S₂), 3,5-dimethyl - 1 N phenyl pyrazole (S₃), 3,5-diphenylpyrazole (S₄) and p-toluene sulfonyl pyrazole (S₅) were prepared by reaction of the corresponding 1,3-dicarbonyl compound with hydrazine or phenylhydrazine⁽¹⁵⁻¹⁷⁾ whereas S₅ was prepared by reaction of pyrazole with p-toluene sulfonyl chloride. The compounds were confirmed by m.p, IR and elemental analysis.

2.2. IR Spectra

The spectra were recorded on a SHMADZU FT-IR Spectrometer in the range $4000-500\text{ cm}^{-1}$, as KBr disc at college of science laboratories- Mesan university.

2.3. X-ray Structure determination

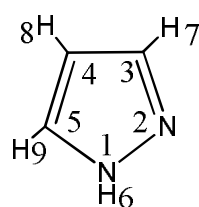
The x-ray diffraction measurements were carried out using single crystal method at 120 K for S_1 and S_4 compounds, at Shaheed paheshty university-Iran . The unit cell dimensions and the geometry parameters have been determined . The crystallographic data analysis gave crystal and molecular structures .

3. Computations

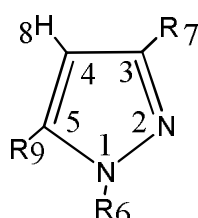
Molecular orbital calculations were performed using ab initio method at MP2 theory / 6-31G(d,p) basis set . The computations were carried out using HperChem software implemented in the HperChem. 8.0 program. Geometry optimization were performed at the same theory level before the calculations of the vibrational frequency. Other physical properties such as total energy, charges on the atoms and dipole moments were also calculated to relate it to structure .

4. Results and discussion

The structural formula with numbering are presented by the following



Where S_1



S_2 : $R_7=R_9=CH_3$, $R_6=H$

S_3 : $R_7=R_9=CH_3$, $R_6=$

S_4 : $R_6=H$, $R_7=R_9=$

S_5 : $R_7=R_9=H$, $R_6=H_3C-$

Fig .1

4.1 Geometry parameters

The calculated geometry parameters for the studied compounds by ab initio method MP2 /6-31G(d,p) are listed in Tables 1 and 2 .

Table 1. Theoretical calculated bonds lengths(\AA) and bonds angles degree for pyrazole and its derivatives using ab initio method MP2/ 6-31G(d,p)

Bond	Compounds				
	S ₁	S ₂	S ₃	S ₄	S ₅
N ₁ -N ₂	1.329	1.338	1.352	1.328	1.339
N ₂ -C ₃	1.301	1.301	1.294	1.305	1.298
C ₃ - C ₄	1.413	1.417	1.408	1.416	1.416
C ₄ - C ₅	1.362	1.365	1.363	1.368	1.358
C ₅ -N ₁	1.341	1.341	1.364	1.345	1.350
N ₁ -R ₆	0.991	0.991	1.428	0.990	1.709
C ₃ - R ₇	1.071	1.501	1.501	1.480	1.071
C ₄ - R ₈	1.069	1.070	1.070	1.067	1.069
C ₅ - R ₉	1.070	1.496	1.566	1.476	1.068

From Table 1 it is clear that the two bonds N₁-N₂ and C₅-N₁ are not equal ,and N₂-C₃ bond is shorter than C₄- C₅. On the other hand C₃- C₄ bond is shorter than that in aliphatic compounds, succinimide and pyrrole . These observations suggest the aromaticity of the pyrazole ring . However substitution of H₆ in pyrazole by phenyl or p-toluene sulfonyl groups increases N₁-N₂ and C₅-N₁ bond lengths. The calculated bond angles(deg.) are shown in Table 2 ,it is clear that the pyrazole molecule is planar, and the two angles N₂-C₃-C₄ and C₃-C₄-C₅ are not equal they are 111.6 and 103.9 deg. Respectively in addition , the dihedral angles in all studied molecules are almost equal to zero which supports the above suggestion.

Table 2 Theoretically calculated bond angles (deg.) in the studied compounds

Angle	Compounds				
	S ₁	S ₂	S ₃	S ₄	S ₅
X ₆ -N ₁ -N ₂	119.3	119.1	115.6	118.3	119.0
X ₆ -N ₁ -C ₅	127.8	127.6	134.0	128.3	128.2
N ₂ -N ₁ -C ₅	112.7	113.1	110.3	113.2	112.6
N ₁ -N ₂ -C ₃	104.9	105.2	107.2	105.6	104.8
N ₂ -C ₃ -C ₄	111.6	110.8	110.3	110.4	111.8
X ₇ -C ₃ -N ₂	120.0	121.2	121.4	121.0	119.9
X ₇ -C ₃ -C ₄	128.2	127.8	128.2	128.4	128.2
C ₃ -C ₄ -C ₅	103.9	104.9	105.7	105.1	104.3
X ₈ -C ₄ -C ₃	128.8	127.8	128.0	127.8	128.0
X ₈ -C ₄ -C ₅	127.8	127.1	126.2	126.6	127.6
N ₁ -C ₅ -C ₄	106.6	105.7	106.4	105.4	106.3

Where X=R

4.2 Same physical properties

The calculated energies : total energy , electronic , nuclear repulsion , HOMO , LUMO and ΔE (in a.u) are listed in Table 3 .

Table 3 Theoretically calculated energies for studied molecules by ab initio method MP2/ 6-31G(d,p).

compound	Total energy[a.u]	Electronic energy[a.u]	Nuclear* repulsion energy	HOMO [e.v]	LUMO [e.v]	ΔE [e.v]
S ₁	-224.803	-389.778	164.97	-9.817	6.225	16.042
S ₂	-302.840	-596.344	293.453	-9.283	6.182	15.465
S ₃	-532.427	-1274.475	742.047	-8.939	3.989	12.928
S ₄	-683.925	-1713.283	1029.358	-8.381	3.417	11.798
S ₅	-965.695	-1934.767	969.072	-9.511	3.462	12.993

* HOMO , LUMO , ΔE in ev

The high occupied molecular orbital energy (HOMO) is in S₁ compound, equals -9.817 a.u. which is the lowest value among the studied compounds. In addition the largest energy gap(ΔE), between LUMO-HOMO also found in S₁ while the smallest gap is in S₄ . From these data one may expect that S₁ has relatively high chemical stability compound with the other studied compounds . This can be explained in term of the substitution effect of phenyl groups in positions 7 and 9 in S₄ .

4.3 Dipole moments and mulliken charges on the atoms

The values of dipole moments and charge on the atoms of studied compounds which are theoretically calculated by ab initio method MP2/ 6-31G(d,p) are shown in Tables 4 and 5 .

Table 4 . The calculated values of dipole moments(in Debye)

Compound	Dipole moment deby	Components		
		X	Y	Z
S ₁	2.4196	-2.2524	-0.8838	0.000
S ₂	2.5659	-2.4294	-0.8257	0.000
S ₃	2.0582	-2.0336	0.3172	-0.0001
S ₄	2.9114	-2.6513	-1.2029	0.000
S ₅	4.0664	0.6752	0.4946	-3.9793

These data suggest the planarity of the compounds except S₅ . On the other hand compound S₅ has the largest value of dipole moment and shows three components of the dipole moment .

From Table 5 , 4-carbon atom in pyrazole carrying the highest negative charge which indicates that the electrophilic reactions occur at this atom . This result is in agreement with the observed electrophilic reaction of pyrazole⁽¹⁴⁾ . In addition , the charge on C₄ is increased in S₃ ,probably due to phenyl group attached to nitrogen atom(N₁)⁽¹³⁻¹⁵⁾ .However , substitution of phenyl groups in 3 and 5 positions reduces the value of the negative charge on C₄ , probably due to sort of conjugation of the phenyl groups with pyrazole ring .On the other hand ,the largest positive charge on carbon atoms in the studied compounds is found on the on C₅ in S₃ compound, 0.38066 (Table 5) . This fact can be understood in term of conjugation of the electron lone pair on the nitrogen atom with phenyl ring .

**Table 5 . Mulliken charges on the atoms of studied compounds
calculated by ab initio method MP2/ 6-31G(d,p).**

Atom no.	Compounds				
	S ₁	S ₂	S ₃	S ₄	S ₅
N ₁	-0.417774	-0.470671	-0.645524	-0.514144	-0.566473
N ₂	-0.313326	-0.356418	-0.354949	-0.373857	0.306062
C ₃	0.094267	0.251618	0.288704	0.27581	0.114670
C ₄	-0.302783	-0.331854	-0.345257	-0.295149	-0.314333
C ₅	0.130365	0.329690	0.380660	0.366222	0.165761
R ₆	0.327422	0.318322	0.344626	-0.324932	1.228664
R ₇	0.152633	-0.343458	-0.342740	-0.024072	0.162433
R ₈	0.155489	0.144825	0.148629	0.158170	0.164775
R ₉	0.173708	-0.357668	-0.343839	0.004945	0.21155

4.4 X-ray Structural determination

X-ray diffraction measurements were carried out on S₁ and S₄ compounds as single crystal at 120 K temperature using x-ray wave length 0.71073 Å. The crystal system of S₁ is orthorhombic with space group Pbcn and the unit cell dimensions are : a=8.2424 Å, b=12.5948 Å, c=6.8159 Å; α=β=γ=90 deg. the crystal of S₄ is monoclinic with space group C_{21c} and the unit cell dimensions are : a=16.886 Å, b=16.959 Å, c=17.5220 Å; α=γ=90 deg. ,β=109.94 deg. The crystal sizes were 0.40x0.30x0.20 mm and 0.25x0.20x0.15 mm for S₁ and S₄ respectively. The values of bond lengths and bond angles determined by x-ray diffractions for the two compounds are listed in Tables 6 and 7.

**Table 6 . Bonds length (Å) and bond angles (deg.) determined
by x-ray diffraction for S₁ compound.**

Bond	Bond length	Angle	Angle value
N ₁ -N ₂	1.351	N ₂ -N ₁ -H ₆	124
N ₂ -C ₃	1.342	C ₅ -N ₅ -H ₆	128
C ₃ - C ₄	1.383	N ₂ -N ₁ -C ₅	108.3
C ₄ - C ₅	1.385	N ₁ -N ₂ -C ₃	108.4
C ₅ -N ₁	1.339	N ₂ -C ₃ -C ₄	109.2
N ₁ -H ₆	0.866	N ₂ -C ₃ -H ₇	125.4
C ₄ - H ₈	0.930	C ₅ - C ₄ -C ₃	104.8
C ₅ - H ₉	0.930	C ₃ -C ₄ -H ₈	127.6
		C ₅ -C ₄ -H ₈	127.6
		C ₄ -C ₅ -N ₁	109.3
		C ₄ -C ₅ -H ₉	125.3
		N ₁ -C ₅ -H ₉	125.3

Table 7 . Bonds length and bond angles (deg.) determined by x-ray diffraction for S₄ compound.

Bond	Bond length	Angle	Angle value
N ₁ -N ₂	1.356	N ₂ -N ₁ -H ₆	125.3
N ₂ -C ₃	1.347	C ₅ -N ₁ -H ₆	125.3
C ₃ - C ₄	1.395	N ₂ -N ₁ -C ₅	109.3
C ₄ - C ₅	1.393	N ₁ -N ₂ -C ₃	108.1
C ₅ -N ₁	1.346	N ₂ -C ₃ -C ₄	108.6
N ₁ -H ₆	0.860	N ₂ -C ₃ -R ₇	122.0
C ₃ - R ₇ ^a	1.472	C ₄ -C ₃ -R ₇	129.2
C ₄ - H ₈	0.930	C ₃ -C ₄ -C ₅	105.7
C ₅ - R ₉	1.473	C ₃ -C ₄ -H ₈	127.1
		C ₅ -C ₄ -H ₈	127.1
		C ₄ -C ₅ -N ₁	107.9
		C ₄ -C ₅ -R ₉	129.5
		N ₁ -C ₅ -R ₉	122.4

a : R₉= R₇= 

It is clear ,from Tables 1 and 2 by comparison with that of Tables 6 and 7 , that the theoretically calculated geometry parameters of S₁ and S₄ compounds are in good agreement with x-ray diffraction results . In addition the calculated and measured dihedral angles for S₁ and S₄ suggest the planarity of the molecules . However , x-ray structural measurements showed presence of hydrogen atoms on both N₁ and N₂ atoms in S₁ compound (Fig.2) . This fact indicates that the compound exists in solid as a tautomeric mixture . It was previously reported that .S₁undergoes tautomerism in solution. On the other hand , x-ray structure of S₄ is shown in Fig.3^(10,12) . It is clear that the

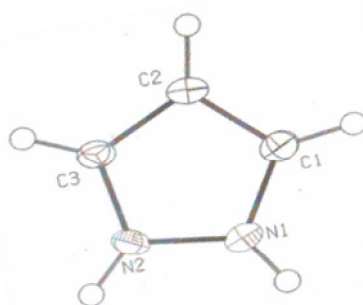


Fig.2 x-ray structure of S₁

S₄ compound does not show tautomerism .

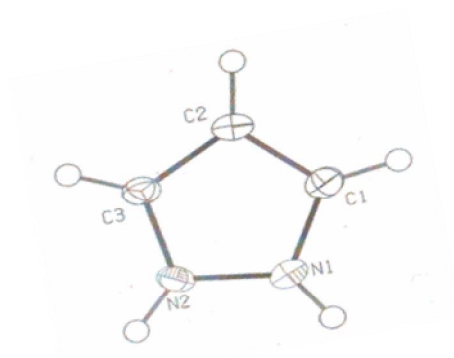


Fig.2 x-ray structure of S₁

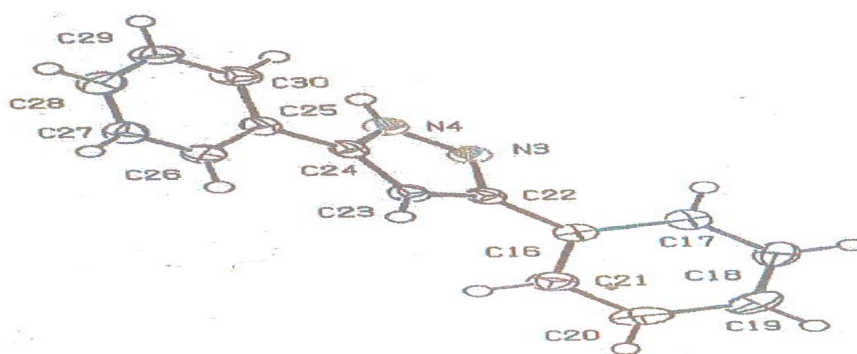


Fig.3 x-ray structure of S₄

In general ,ab initio calculations for the bond lengths ,N₂-C₃ , C₄-C₅ , N₁-N₂ ,in S₁ and S₄ compounds give slightly smaller values than that determined by x-ray analysis except that of C₃-C₄ bond. However ,x-ray determination showed the bond lengths , N₂-C₃ ,C₃-C₄ ,C₄-C₅ and N₁-N₂ in S₄ are longer than that of S₁ .

4.5 IR spectra

The theoretically calculated IR frequencies by ab initio method for the studied compounds are shown in Table 8 and 9 .

Table 8 . Theoretical (an initio method MP2 / 6-31G(d,p)) and experimental IR data for pyrazole and 3,5-dimethyl pyrazole .

Pyrazole			3,5-dimethyl pyrazole		
Ferquency cm ⁻¹	Approximative description	Exp. cm ⁻¹	Ferquency cm ⁻¹	Approximative description	Exp. cm ⁻¹
3714	NH st	3200 broad	3710	NH st	3207 broad
3248	=C-H sst	3100	3221	=C-H st	3107
3230	=C-H ast	3040	3084	C-H ast	2943
3217			3076	C-H sst	2901
1647	NH δ ip, C=N st, C-H δ ip	1716	1678	NH δ ip , C=N st , C-H δ ip	1662
1545	NH δ ip, C-N st , C-H δ ip	1556	1590		1592
1462	C=C st, N=C st , C-H δ ip	1467	1543	NH δ ip , C-N st , C-H δ ip	1552
1457	N-C st , N=C st , C-H δ ip	1447	1512	C=C st , N=C st , C-H δ ip	1485
1325	N-C st , C=N st , C-H δ ip	1396	1451	N-C st , N=C st , C-H δ ip	1465
1209	Ring s , C-H δ oop	1140	1322	N-C st , C=N st , C-H δ ip	1423
1160	C-N st , C-H s	1130	1197	Ring s , C-H δ oop	1379
1076	C-H δ ip , N-N st	1050	1094	C-N st , C-H s	1307
1067	C-H δ ip , N-N st	1010	1161	C-H δ ip , N-N st	1267
966	C=N-N s C-H δ ip	990	1066	C-H δ ip , N-N st	1155
958	C-C=N s , C-H δ ip	937	1005	C=N-N s , C-H δ ip	1149
939	C-H δ oop	769	838	C-C=N s , C-H δ ip	1028
928	C-H δ oop		748	C-H δ oop	1010
806	C-H δ oop		704	C-H δ oop	779
704	N-H δ oop , C-H δ oop	750			
650	N-H δ oop	638			
553	N-H δ oop	575			

a Scaled by 0.9427

b KBr disc

c Vibrational modes : st. stretching , sst. Symmetrical stretching , ast. asymmetrical stretching , δ deformation , ip. in plane bending , oop. out of plan bending .

**Table 9 . Theoretical(ab initio method MP2 / 6-31G(d,p))
for S₄ and S₅ compounds in the range 4000- 1400 cm⁻¹.**

S ₄ ν^a cm ⁻¹	S ₅ ν cm ⁻¹
3735	3284
3203	3257
3196	3097
1715	1703
1692	1693
1680	1636
1662	1579
1577	1542
1556	1538
1528	1486
1525	1468
1482	1378
1472	1370
1394	

^a Scaled by 0.9427

In general the calculated IR values of the studied molecules are in good agreement with the experimental . From Tables 8 and 9 substitution of phenyl group (as in S₄) increases the NH frequency whereas substitution of methyl group (as in S₅) reduces its value ,compound by pyrazole . The increase can be explained in term of conjugation of the phenyl group with NH while the decrease is due to inductive effect of CH₃ group . However , NH in plane bending frequency also shifts to higher frequency by phenyl and methyl groups . In these molecules , the vinyl hydrogen stretching appears at higher frequency compound with that of the aromatic hydrogens.

4.6 Conclusion

ab initio calculations for geometrical parameters and vibrational frequencies for pyrazole and substituted pyrazole are in good agreement with experimental . The x-ray data analysis indicates existence of pyrazole as a tautomeric mixture in the solid state whereas 3,5-dimethyl pyrazole is not.

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