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Synthesis and spectral studies of 2-amino-1,4-naphthoquinone

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Abstract : 2-amino-1,4-naphthoquinone was synthesized. The vibrational wave numbers of this compound have been calculated using Gaussian 09 software code, employing Density Functional Theory. The IR data is compared with experimental values. The predicted infrared intensities and Raman activities are reported. The calculated frequencies are in good agreement with the experimental values. The calculated geometrical parameters are also given. The study is extended to calculate the HOMO-LUMO energy gap, Ionization potential (I), Electron affinity (A), Global hardness (η), chemical potential (μ) and global electrophilicity (ω). The calculated HOMO-LUMO energies show the charge transfer occurs in the molecule. Optimized geometrical parameters of the title compound are in agreement with similar reported structures.
Keywords : 2-amino, 3-chloro 1,4-naphthoquinone, IR, DFT, Energy gap.

Introduction :

Quinone moieties are present in many drugs, such as antracylines, claunorubicin, doxorubicin, mitocin, mitoxanthrones and saintopin, which are used clinically in anticancer therapy. 1,4-Naphthoquinones, possessing an amino or a substituted amino group in the 2-position, have been a subject of study for many years because of their use in a variety of medical and biological applications, including as antituberculars, antimalarials, antibacterials, antitumor agents, larvicides and molluscicides, herbicides, and fungicides [1-5].Quinones and their derivatives are substances naturally obtained or synthesized in the laboratory [6] with multiple biological functions in the metabolic cycles of various organisms [7-8]

1,4-Naphthoquinones, possessing an amino or a substituted amino group in the 2-position, have been a subject of study for many years because of their use in a variety of medical and biological applications, including as antituberculars, antimalarials, antibacterials, antitumor agents, larvicides and molluscicides, herbicides, and fungicides [9-11] The introduction ofamino substituents onto the quinone moeity can exert influence on its redox properties, inducing oxidative stress in cells and alkylation of DNA. The aminoquinones are found in important bioactive compounds such as antimalarial agents (12).2-Amino-1,4-naphthoquinone have been synthesized by various methods (13)

This paper describes synthesis and vibrational spectra of 2-amino,3-chloro 1,4-naphthoquinone calculated by DFT basis set, the data is compared with experimental values. The wave number values computed by the HF method and 6-31 G* level contain known systematic errors due to negligence of electron correlation. We therefore have used the scaling factor as 0.90 for HF/6-31G* set. Geometrical parameters, Mulliken atomic charges and HOMO – LUMO energy gap of the chelate is reported.

2. Materials and Methods

The Synthesis of 2-Amino-1,4-naphthoquinones: To a stirred solution of naphthoquinone(1.8 mmol) in 15 mL of methanol under argon was added asolution of sodium azide (10.6 mmol) in 5 mL of water, acidifiedto pH 4 (with 1 N HCl). The reaction was stirred at room temperature (or 50°C) and monitored by TLC and then the mixture was extractedtwice with EtOAc and the combined organic layers werewashed with water and brine, dried over Na2SO4, and concentrated. The residue was crystallized from an ether-hexanemixture.

2.1Instrumental Analysis

Elemental analysis was carried out with a Perkin Elmer 2400 series for C, H, and O & N. The IR spectra were recorded on a JASCO FTIR spectrophotometer model in a KBr matrix and in the range of 4000 – 400 cm^{-1}.

2.2.1 Computational details

The entire calculations conducted in the present work were performed DFT method and fr5equncy-RB3LYP with LANL2DZ basis set in the Gaussian 09 software code. The geometries were first determined at the Density functional theory level of employing SDD basis set . The wave number value computed theoretically contains known systematic error due to the negligence of electron correlation. We have used the scaling factor value of 0.9393 for HF /SDD basic set. The absence of imaginary wave number on the calculated Vibrating Spectrum confirms that the structure corresponds to minimum energy. HOMO-LUMO energy gap and other related molecular parameters are calculated.

3. Results and Discussion

About 51 infra-red bands in the **2**-amino - 1,4-naphthoquinone have been observed in the calculation by DFT method .The wave numbers of all the calculated and observed frequencies are given in Table 1. The probable modes of vibrations assigned for the observed frequencies are given in the last column of the table. The assignments of the fundamental frequencies made on the basis of intensity considerations and position of observed frequencies.

Table 1 : IR frequencies calculated and observed of 2-amino-1,4-naphthoquinone

Sr. No.	Frequency cal. cm^{-1}	In. cal. km / mol	Raman Activity -A^4	Obd. cm^{-1}	In. Ob. % T	Assignments
1	94.02	0.09	0.41	--	--	C-H & N-H Stretching O.P.
2	159.14	0.22	1.17	--	--	C-H Streching O.P.
3	187.12	5.20	2.00	--	--	C-N Bending
4	277.04	5.83	1.48	--	--	C=O Bending
5	328.54	11.68	2.11	--	--	C-N & C-O I.P.
6	396.35	1.42	0.29	--	--	C-H Stretching O.P.
7	410.59	5.49	2.19	--	--	C=O Bending
8	425.13	4.73	0.11	--	--	C-H Bending O.P.
9	437.25	23.67	3.26	--	--	C=O Bending
10	467.29	0.92	1.25	471.51	57.08	C-H & N-H Bending
11	482.43	14.71	16.82	509.115	67.66	C-H Bending I.P.
12	548.77	0.67	32.39	--	--	C-H Bending I.P.
13	639.47	167.97	9.81	606.503	83.89	C=O Bending
14	651.67	36.52	2.56	--	--	C-H & N-H Bending
15	668.48	12.20	7.82	662.428	84.04	C-H & N-H Bending
16	682.68	9.91	5.24	--	--	C=O Bending
17	702.80	37.16	7.85	--	--	N-H Bending
18	723.46	21.99	1.35	726.068	78.23	C-H Bending
19	753.07	48.77	1.72	--	--	C-H & N-H Bending
20	775.15	8.36	55.70	778.136	83.37	C=C Stretching

21	848.60	10.40	0.50	833.098	87.04	C=O Stretching
22	861.27	4.36	0.52	--	--	C-H Bending
23	866.84	14.36	2.11	--	--	C-H Bending
24	960.96	1.35	0.02	--	--	C-H Bending
25	973.94	0.09	0.18	--	--	C-H Bending
26	975.55	25.11	23.48	985.447	85.02	C-H Bending
27	1039.53	1.41	14.48	--	--	C-H Bending
28	1101.98	3.28	1.09	--	--	C-H Bending
29	1134.14	4.34	13.65	1127.19	88.58	N-H Bending
30	1146.79	12.79	20.96	--	--	N-H Bending
31	1152.25	2.88	11.75	--	--	C-H Bending
32	1240.53	12.81	16.59	1219.76	87.11	C=O Stretching
33	1251.75	3.66	33.76	1271.82	78.76	N-H Stretching
34	1324.31	21.96	10.13	--	--	C=C Stretching
35	1334.30	2.86	3.01	1364.39	78.70	C=C Stretching
36	1438.03	30.88	9.48	1418.39	83.19	C=C Stretching
37	1453.59	1.43	14.66	--	--	C=C Stretching
38	1492.69	88.17	12.28	--	--	C=O Stretching
39	1562.58	59.50	2.09	1566.88	73.92	C=C Stretching
40	1589.27	359.00	3.40	--	--	C=O Stretching
41	1598.34	76.64	8.01	--	--	C=C Stretching
42	1601.51	55.95	19.32	--	--	N=H Stretching
43	1642.27	206.59	34.69	--	--	N=H & C=C Stretching
44	1665.81	1.42	130.94	1685.48	81.72	N=H & C=C Stretching
45	3113.03	770.26	770.26	3189.68	92.11	C-H Stretching O.P.
46	3303.44	54.41	59.41	--	--	C-H Stretching O.P.
47	3315.54	2.16	71.26	--	--	C-H Stretching I.P.
48	3323.80	0.02	32.00	--	--	C-H Stretching I.P.
49	3328.30	0.74	34.52	3387.35	89.62	C-H Stretching O.P.
50	3581.02	16.72	116.56	3575.20	78.36	N=H Stretching O.P.
51	3770.65	30.37	49.08	--	--	N=H Stretching

C--H stretching frequencies: ν (C-H) of this ligand frequencies are predicted at 3328.20, 3323.80, 3315.54, 3303.44 and 3113.03cm^{-1} by DFT theory. The observed frequencie is at3387.35 cm^{-1}only.

C—C stretching frequencies: The C—C stretching vibrations of this compound are in the region 1357 – 1650 $cm^{-1}$for **2-**amino-1,4-naphthoquinone. The predicted frequencies are at 1324.31, 1334.30, 1438.03, 1453.59 and 1562.58 cm^{-1} and the observed frequencies in recording IR spectrum are at 1364.39, 1418.39 and 1566.88cm^{-1} .which have been taken as totally symmetric a_1 type of vibrations. In addition to these , the vibration at 1453.59 m^{-1} have been taken as such, corresponding to 1460 cm^{-1} (a_{ge}) of naphthalene.

C—N stretching frequencies: In nitroso naphthoquinone compounds nitrogen is directly attached to the ring and the stretching vibration of the phenyl carbon nitrogen bond is expected in the range of 1330 -1260$cm^{-1.}$ We observed this υ CN mode at 1271.82cm^{-1}in IR recorded spectrum and 1251.75 and 1324.31cm^{-1} in DFT calculations.

N-H bending frequencies: In amino compounds N—H bending frequencies are observed at 471.51, 662.42 and 1127.19cm^{-1} and DFT predicted frequencies are at 467.29, 651.67, 668.48, 702.80, 1134.14 and 1146.79 cm^{-1}.

C- Substituted vibrations : C=O group frequencies, in the stretching region of the infra red spectra of **2-**amino-1,4-naphthoquinone are predicted at 868.60, 1240.53, 1492.69 and 1589.272 cm^{-1} while only two bands have been observed at 833.09 and1219.76 cm^{-1}.

C=O group frequencies, in the bending region of the infra red spectra of **2-**amino-1,4-naphthoquinone are predicted at 277.04, 410.59, 437.25, 410.59, 432.25, 639.47and 682.68 cm^{-1} while only one band have been observed at 606.50 cm^{-1}

The C-H bending out of plane vibrations : The C-H bending out of plane vibrations are predicted at 396.35, 425.13, 482.43, 548.77, 861.27, 866.84, 960.96, 973.94, 975.55, 4039.57, 1101.98 and 1152.25cm^{-1} for **2-**amino-1,4-naphthoquinoneand we observed bands at 509.11 and 985.44 cm^{-1}.

C-H stretching frequencies: The C-H stretching vibrations are predicted at 3113.03, 3303.44, 3323.80, 3328.30 and 3315.30 cm^{-1} for **2-**amino-1,4-naphthoquinone and we found only one band at 3189.68 cm^{-1} .

N-H stretching frequencies: The N-H stretching vibrations are predicted at 3581.02and 3770.65 cm^{-1} for **2-**amino-1,4-naphthoquinone and we found only one band at 3575.20 cm^{-1}

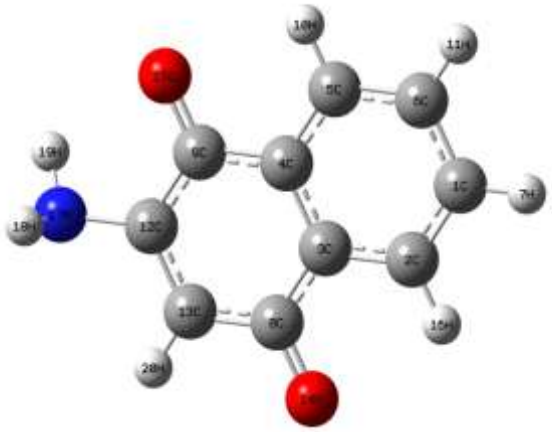

Fig. 1Molecular structure of 2-amino-1,4-naphthoquinone

Molecular geometry:

The optimized structure parameters of **2-**amino-1,4-naphthoquinone calculated by ab initio, DFT basis set are listed in Table 2 in accordance with the atom numbering scheme given in Fig -1. The values of bond length in A^0, and bond angles in degree are given in Table 2.

Table No:-2 Bond Length and Bong Angle of 2-amino-1,4-naphthoquinone

Bond Length	A^0	Bond Angle	0
N17H19	1.000	H19N17H18	109.47
N17H18	1.000	H19N17C12	109.47
C12N17	1.470	H18N17C12	109.47
C12C13	1.401	C12C9O15	120.00
C12C9	1.401	C4C9O15	120.00
C9O15	1.258	C13C8O14	120.00
C9C4	1.401	C3C8O14	120.00
C4C3	1.407	--	--
C8C3	1.401	--	--
C8O14	1.258	--	--
C13H20	1.070	--	--
C3C2	1.401	--	--
C2C1	1.401	--	--
C1C6	1.404	--	--
C5H10	1.070	--	--

Mulliken charges arise from the Mulliken population analysis (14) and provide a means of estimating partial atomic charges from calculations carried out by the methods of computational chemistry, particularly those based on the linear combination of atomic orbital's molecular orbital method, and are routinely used as variables in linear regression QSAR procedures.In the application of quantum mechanical calculation to molecular system, the calculation of effective atomic charges plays an important role. The electron distribution of **2-**amino,3-chloro 1,4-naphthoquinoneis compared in the two different mechanical methods and the sensitivity of the calculated charges to charge in choice of methods is studied. By determining electron population of each atom in the defined basis function, the Mulliken charges are calculated by DFT/SDD. The results are presented in Table-3 which the values of atomic charges of each atom of the concerned molecule (15).

Table-3:- Mulliken Atomic Charges of 2-amino-1,4-naphthoquinone

Sr. No.	Atom	Atomic charge
1	C	-0.307018
2	C	0.285474
3	C	0.248399
4	C	0.127196
5	C	0.235325
6	C	-0.290846
7	H	0.139684
8	C	-0.391477
9	C	-0.748651
10	H	0.158230
11	H	0.139010
12	C	0.316261
13	C	0.242258
14	O	-0.278238
15	O	-0.271080
16	H	0.160194
17	N	-0.433364
18	H	0.264394

Table No: - 4 Comparison of HOMO-LUMO, Energy gap and related Molecular Properties of 2-amino-1,4-naphthoquinone

Molecular Properties	DFT
HOMO eV	-0.27088
LUMO eV	-0.14675
Energy gap	0.12413
Ionisation Potential (I)	-0.14675
Electron Affinity(A)	-0.27088
Global Hardness (η)	0.06200
Chemical Potential (μ)	0.20881
Global Electrophilicity (ω)	0.70254

HOMO-LUMO energy gap and related molecular properties.

The HOMO-LUMO energy gap of the molecule **2-**amino-1,4-naphthoquinonein the DFT and SDD basis set has been calculated. The HOMO-LUMO energy gap is constant in both methods. It is known that the value of E_{HOMO} is often associated with the electron donating ability of inhibitor molecule, higher values of E_{HOMO} is an indication of the greater ease of donating electrons to the unoccupied orbital of the receptor. The value of E_{LUMO} is related to the ability of the molecule to accept electrons, lower values of E_{LUMO} shows the receptor would accept electrons. Consequently, the value of *Egap* provides a measure for the stability of the

formed complex on the metal surface. The frame work of SCF MO theory, the ionization energy and electron affinity can be expressed through HOMO and LUMO energies AS I= -E_{HOMO}, A= -E_{LUMO}. The hardness compounds to the gap between the HOMO and LUMO orbital energies. If the gap energy is higher than the Hardness is also larger. The global hardness $\eta = \frac{1}{2}(E_{HOMO} - E_{LUMO})$. The hardness is associated with the stability of chemical potential (μ) can be expressed in combination of electron affinity and ionization potential. The global electrophilicity index ($_{\omega}$) is also calculated (16) and listed in table- 4.

(a) HOMO **(b)LUMO**

Fig. 2 : a) HOMO and b)LUMO of 2-amino-1,4-naphthoquinone

Thermodynamic properties

On the basis of vibrational analysis at B3LYP / SDD level, several thermodynamic parameters are calculated and are presented in Table-5. The zero point vibration energy (ZPVE) and the entropy, Svib.(T) are calculated to the extent of accuracy and the variations in ZPVE seem to be insignificant. The total energy and the change in total entropy of **2-**amino,3-chloro 1,4-naphthoquinoneat room temperature at different methods is only marginal (17-18).

Table 5 Theoretically computed Energies (a.u.), Zero point Energy (Kcal / mol) Rotational Constants (GHz),Entropy (cal $mlo^{-1}K^{-1}$) and Dipole moment D (Kcal. $mlo^{-1}K^{-1}$)

Parameter	DFT/B3LYP/SDD
Total Energy e.u.	-590.607 a.u.
Zero Point Energy	381660.3 (Joules/Mol)
Rotational constants(GHZ)	1.3150345 0.7977266 0.4976128
Entropy Total	92.760
Translational	41.353
Rotational	30.799
vibrational	20.608
Dipole movement (D)	2.3807 Debye

4. Conclusions

This ligand has four donating atoms which are useful for biological various reactions. The calculated vibration frequencies are compared with experimental data and found most of them are in good agreement. The assignments were confirmed with the help of animation process which is available in Gaussian 09 computer code. The molecular geometry of **2-**amino-1,4-naphthoquinoneisbest at the DFT/ SDD level. The HOMO-LUMO energy was calculated and other related molecular properties were also discussed. The Mullikan atomic charges were calculated and the results were discussed. Thermodynamic parameters were calculated.

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