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Vibrational Spectroscopic Investigation and Theoretical Calculations of (E)-3-Phenyl-N-[4-(Phenyl-Amino) Quinazoline-7-yl] Acrylamide

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Vibrational Spectroscopic Investigation and Theoretical Calculations of (E)-3-Phenyl-N-[4-(Phenyl-Amino) Quinazoline-7-yl] Acrylamide

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Address correspondence to Qing Zheng, Department of Chemical and Biological Engineering, Yancheng Institute of Technology, Yancheng 224003, P. R. China. E-mail: zhengging0508@163.com **ABSTRACT** Optimized geometrical structure and harmonic vibration frequencies of prior synthesized (E)-3-phenyl-N-[4-(phenyl-amino) quinazoline-7-yl] acrylamide were computed by ab initio HF and DFT/B3LYP methods using both 6-31G* and 6-311G** basis sets and the Moller–Plesset second-order perturbation (MP2) method merely at the 6-31G* level. The infrared (IR) spectrum of the title compound has been measured in the range of 400–4000 cm⁻¹. Complete vibrational assignments of the IR spectra were proposed. Moreover, the calculated wavenumbers of the title compound were compared with the experimental data. The correlation analyses indicate that good linearity relationships exist between the scaled theoretical vibration frequencies and the experimental values. Additionally, the atoms in molecules (AIM) method was applied to explore the possible intramolecular interactions in the title compound.

KEYWORDS atoms in molecules (AIM) method, B3LYP, HF, IR spectra, MP2, (E)-3-phenyl-N-[4-(phenyl-amino) quinazoline-7-yl] acrylamide

INTRODUCTION

The 4-anilinoquinazoline derivatives have proven to be highly potent and selective among the many reported classes of protein kinase inhibitors.^[1–3] These compounds have been identified as potential anticancer drugs since they are inhibitors of the ErbB family of receptor tyrosine kinases (epidermal growth factor receptor [EGFR], ErbB2 and ErbB4).^[4–6] By restraining EGFR produced via abnormal signal transduction owing to hyperactivation of tyrosine protein kinases as a result of overexpression or mutation, anticancer activities against human squamous head and neck carcinomas, lung cancer, and breast cancer are brought about.^[7] Moreover, based on the 4-anilinoquinazoline scaffold, three ErbB family-directed inhibitors (Tarceva, gefitinib, and lapatinib) have been clinically approved for treating certain types of cancer.

A considerable amount of studies have been conducted on various properties of 4-anilinoquinazoline derivatives. For example, Hennequin et al.^[8] investigated the structure-activity relationship of a novel subseries of 4-anilinoquinazoline EGFR inhibitors substituted at the C-6 position with carbon-linked side chains. The binding mode of the 4-anilinoquinazoline class of protein kinase inhibitor has been studied by Shewchuk et al.^[9] Gayani and co-workers^[10] reported the design and synthesis of a set of "clickable" 4-anilinoquinazoline kinase inhibitors. Chandregowda et al.^[11] synthesized a series of 6,7-dialkoxy-4-anilinoquinazolines and checked their anticancer activities. Meanwhile, some threedimensional quantitative structure-activity relationships (3D-QSARs) for 4-anilinoquinazoline compounds have also been presented.[12,13] However, there is little research on their vibration spectra, which might be useful for the design of novel inhibitors. Vibrational spectroscopy is of practical importance to confirm the identity of a completely new molecule as well as to derivate the thermochemical and kinetic information. This work can be of reference value to study spectral properties of similar compounds.

Ab initio Hartree-Fock (HF) and density functional theory (DFT)/B3LYP are at present widely used methods for simulating molecular vibration spectra. For instance, the HF and B3LYP calculations for 2-chlorotoluene and 2-bromotoluene showed excellent agreement with the observed IR spectra.^[14] Ramoji et al.^[15] reported that the simulated vibrational spectra of 3-acetyl-6-bromocoumarin and 3-acetyl-6-methylcoumarin with HF and B3LYP methods were quite close to the corresponding experimental frequencies. Nagabalasubramanian et al.^[16] further confirmed the success of the HF and B3LYP methods in exploring the IR spectra for 1,5-methylnaphthalene. Furthermore, Møller-Plesset perturbation theory (MP) is one of several quantum chemistry post-Hartree-Fock ab initio methods in the field of computational chemistry. It improves on the Hartree-Fock method via adding electron correlation effects by means of Rayleigh-Schrödinger perturbation theory (RS-PT), usually to second (MP2) order.

This paper is an attempt to thoroughly study the IR spectrum of (E)-3-phenyl-N-[4-(phenyl-amino) quinazoline-7-yl] acrylamide prepared in advance.

Geometrical parameters, atomic charges, vibrational wavenumbers, and modes of vibrations of the title molecule were investigated using HF and DFT/ B3LYP methods with both 6-31G* and 6-311G** basis sets and the Moller–Plesset second-order perturbation (MP2) method merely at the 6-31G* level. The experimental IR spectrum of the title compound was measured and analyzed. In addition, the experimental values were compared with the theoretical ones. Moreover, the atoms in molecules (AIM) method was applied to investigate the possible intramolecular interactions in the title compound, which might result in the shifts of vibrational frequencies.

EXPERIMENTAL DETAILS

Synthesis of the title compound involved the following steps:

2-Amino-4-nitro-benzoic acid (0.005 mol, 0.91 g), formamidine acetate (0.0075 mol, 0.78 g), and ethanol (20 mL) were mixed and heated to reflux for 24 hr. The reaction mixture was then left to cool down. The formed precipitates were filtered to give 7-nitro-quinazoline-4-ketone (0.70 g). Yield: 73.3%.

7-Nitro-quinazoline-4-ketone (0.01 mol, 1.91 g), thionyl chloride (20 mL), two drops of DMF, and 1,2-dichloroethane (4 mL) were mixed and heated to reflux for 4 hr. After cooling to room temperature, the reaction mixture was poured onto crushed ice. The resulting suspension was filtered, washed with water to neutrality, and dried with an infrared oven to give 4-chloro-7-nitro-quinazoline (1.74 g). Yield: 82.58%.

4-Chloro-7-nitro-quinazoline (0.01 mol, 2.10 g), aniline (2.73 mL), and isopropyl alcohol (50 mL) were mixed and heated to reflux for 2 hr. The reaction mixture was then put into the fridge and allowed to stand overnight. 4-Phenyl-amino-7-nitro-quinazoline hydrochloride (2.06 g) was collected by filtration. Yield: 68.2%.

4-Phenyl-amino-7-nitro-quinazoline hydrochloride (0.002 mol, 0.61 g), ethanol (16 mL), water (12 mL), iron (0.01 mol, 0.56 g), and glacial acetic acid (4 mL) were mixed and heated to reflux at 81°C for an hour. The filtrate obtained by filtration of the reaction mixture was concentrated, adjusted to pH=8 with saturated aqueous sodium carbonate solution, and then filtered. The resulting filter cake was dried and recrystallized from a mixture of ethanol and water (1:1) to give 4-phenyl-amino-7-amino (0.34 g). Yield: 71.7%.

Cinnamic acid (0.001 mol, 0.148 g) was dissolved in pyridine (5 mL) under stirring at room temperature. Then, benzenesulfonyl chloride (0.001 mol, 0.127 mL) was dropwise added into the solution; the temperature was controlled at 0°C throughout the whole process. The reaction mixture was stirred for 15 min at room temperature until it became viscous. After cooling to 0°C with an ice bath, 4-phenylamino-7-amino quinazoline (0.001 mol, 0.236 g) in 5 mL of pyridine and dimethylaminopyridine (0.06 g) were added into the solution. The mixture obtained was slowly stirred at room temperature. The reaction endpoint was monitored by thin-layer chromatography (TLC), with the reaction time being 1.5 hr. The reaction solution was then poured into ice-cooled water under agitation. The resulting light yellow suspension was filtered, washed with water to neutrality, dried over anhydrous magnesium sulfate, and recrystallized from a mixture of methanol and ethanol to give the crude product (0.125 g) as buff amorphous powder. Yield: 34.1%, m.p. 266.8-269.9°C.



FIGURE 1 Observed ¹H-NMR spectrum of (E)-3-phenyl-N-[4-(phenyl-amino) quinazoline-7-yl] acrylamide in CDCl₃. (color figure available online.)

The solid sample was dissolved in standard CDCl_3 solvent. Then, the ¹H NMR spectra were measured at 400 MHz on a Bruker Avance NMR spectrometer, with TMS as the internal reference. The observed ¹H NMR spectra is denoted in Fig. 1. The IR spectrum was recorded on a Nexus 470 FT-IR spectrophotometer in the range of 400–4000 cm⁻¹ at room temperature using the KBr pellet technique. The spectral resolution is $\pm 2 \text{ cm}^{-1}$.

QUANTUM CHEMICAL CALCULATIONS

The entire quantum chemical calculations were performed with the Gaussian 03 program,^[17] using both the HF and B3LYP methods at the 6-31G* and 6-311G** level of theories and the MP2 method merely at the 6-31G* level. For the theoretical wavenumbers, the scaling factors have been introduced to compensate for the errors arising from vibrational anharmonicity and basis set incompleteness. The assignments of the vibrational frequencies have been made on the basis of the Gaussview program.^[18] In addition, the AIM method was applied to study the possible intramolecular interactions in the title compound. The AIM analysis was performed with the AIM2000 software,^[19] using the wave function obtained by the B3LYP/6-31G* method for an example.

RESULTS AND DISCUSSION Molecular Geometry

The optimized geometry with numbering of atoms for the title compound is shown in Fig. 2. In the current paper, phenyl rings of C1C2C3C4C5C6, C12C14C15C16C17C13, and C23C24C25C26C27C28 are designated as PhI, PhII, and PhIII, respectively. Qring stands for quinazoline ring. The structure was found to be minimal on the potential energy surface since there is no imaginary frequency. The global minimum energy obtained by the HF, DFT, and MP2 methods with the 6-31G* basis set for the title molecule is -1174.151465, -1181.549309, and -1174.140 a.u., respectively. At the 6-311G** level, the corresponding value with the HF and DFT methods is -1174.404218 and -1181.838810 a.u., respectively. The selected theoretical structural parameters



FIGURE 2 Optimized geometry with atomic numbering and molecular graph of (E)-3-phenyl-N-[4-(phenyl-amino) quinazo-line-7-yl] acrylamide. (color figure available online.)

(bond lengths, bond angles, and dihedral angles) are summarized in Table 1. In this work, geometry optimization parameters have been obtained by assuming Cs point group symmetry. Obviously, the corresponding structural parameters are almost equal to each other with the same exchange function. For different exchange functions, bond angles calculated by the three methods were almost consistent with each other, but the bond lengths were found to be slightly shorter in case of HF calculation with respect to those of both the B3LYP and MP2 methods, due to the neglect of electron correlation. Except for the two dihedral angles N21C18N20C23 and H40N20C23C24, the B3LYP method gave almost the same dihedral angles as the HF method. Compared with the other two methods, the MP2 calculations totally had large deviations in the prediction of the dihedral angles; the cases of the C5C7C8C9 and C7C8C9O11 dihedral angles were the two exceptions.

For the title compound, the electron density topological graph obtained on the optimized wave function by the B3LYP method at the $6-31G^*$ level was also illustrated in Fig. 2, in which the ring critical points were represented with the yellow points, while the bond critical points were denoted with the red points. Obviously, there are four kinds of intramolecular weak interactions in (E)-3-phenyl-N-[4-(phenyl-amino) quinazoline-7-yl] acrylamide, namely, N(21)...H(42), H(39)...H(40), O(11)... H(37), and H(32)...H(35) interactions. Moreover, the AIM calculations by the other four methods showed similar results.

Atomic charges affect dipole moment, molecular polarizability, electronic structure, and other properties of molecules. As a result, it is necessary to consider Mulliken atomic charges in applying quantum chemical calculation to the molecular system. The total atomic charges obtained by Mulliken population analysis are listed in Table 2. From Table 2, it is seen that the charge changes with basis set. For example, the charge of O (11) atom is -0.377 e for B3LYP/6-311G**, -0.523 e for B3LYP/6-31G*, -0.505 e for HF/6-311G**, -0.624 e for HF/ 6-31G*, and -0.649 e for MP2/6-31G*. Considering all the methods and basis sets used in the atomic charge calculation, hydrogen atoms exhibit positive charge, which are acceptor atoms, whereas negatively charged carbon atoms are donor atoms. The negative values on N and O atoms lead to a redistribution of electron density.

Vibrational Analysis

Vibrational spectroscopy has proven to be effective in refining chemical structures and investigating reaction kinetics of organic compounds.^[20,21] The experimental frequencies with their probable assignments are given in Table 3. The observed IR spectrum is shown in Fig. 3. The detailed vibrational assignments of (E)-3-phenyl-N-[4-(phenyl-amino) quinazoline-7-yl] acrylamide are briefly illustrated herein.

C–H Vibrations

The characteristic C–H stretching vibrations of the phenyl ring are expected to appear in the range of $3100-3000 \text{ cm}^{-1}$.^[22] The bands in this region are not affected appreciably by the nature and position of the substituents.^[23] Two medium strong bands observed at 3030 and 3056 cm^{-1} in experimental IR spectra are the results of the coupling of the C-H stretching vibration of the phenyl ring I and C-H stretching of H-C(7) = C(8)-H.

The C–H in-plane bending vibrations usually occur in the region $1000-1300 \text{ cm}^{-1}$ and are very useful for the identifications of structural groups.^[24] One infrared band at 1248 cm^{-1} with medium strong intensity and two weak infrared bands at 994 and

TADIE 1	Ontimized Decemeters of	(E) 2 Dhonyd N	[4 (Dhonyl Amino) Ouineraline 7 vll	Aandomida
IADLL I	Optimized Parameters of	(E)-3-Prienyi-in-	[4-(Fnenyi-Aniino) Quinazonne-7-yij	Acrylannue

Parameters	HF/6-31G*	HF/6-311G**	B3LYP/6-31G*	B3LYP/6-311G**	MP2/6-31G*
Bond length (Å)					
R(4,5)	1.396	1.395	1.409	1.406	1.406
R(5,6)	1.392	1.390	1.407	1.404	1.405
R(5,7)	1.473	1.473	1.462	1.462	1.463
R(7,8)	1.327	1.325	1.346	1.342	1.347
R(8,9)	1.487	1.489	1.484	1.485	1.485
R(9,10)	1.369	1.369	1.388	1.386	1.381
R(9,11)	1.201	1.194	1.227	1.220	1.234
R(10,12)	1.400	1.400	1.403	1.402	1.406
R(12,13)	1.419	1.418	1.421	1.419	1.418
R(14,12)	1.370	1.369	1.388	1.386	1.387
R(13,17)	1.361	1.360	1.378	1.376	1.382
R(14,15)	1.406	1.406	1.409	1.407	1.408
R(15,16)	1.400	1.398	1.425	1.422	1.419
R(16,17)	1.412	1.411	1.414	1.412	1.413
R(15,19)	1.362	1.362	1.372	1.370	1.375
R(16,18)	1.442	1.442	1.446	1.445	1.439
R(18,20)	1.358	1.357	1.370	1.368	1.374
R(18,21)	1.302	1.300	1.328	1.324	1.327
R(20,23)	1.412	1.410	1.410	1.410	1.411
R(21,22)	1.344	1.344	1.354	1.353	1.361
R(23,24)	1.390	1.389	1.404	1.401	1.402
R(22,19)	1.287	1.285	1.312	1.309	1.318
R(23,28)	1.391	1.393	1.407	1.405	1.403
Bond angle (°)					
A(4,5,6)	118.4	118.4	118.1	118.1	118.7
A(5,7,8)	127.9	128.0	128.1	128.2	126.1
A(7,8,9)	119.7	119.6	119.9	119.9	119.6
A(8,9,10)	113.3	113.1	113.2	113.0	113.0
A(8,9,11)	122.8	122.9	123.3	123.4	123.1
A(10,9,11)	123.8	124.0	123.5	123.6	123.9
A(9,10,12)	129.6	129.5	129.5	129.5	128.8
A(13,17,16)	122.0	122.0	122.0	122.0	121.3
A(15,16,17)	118.3	118.3	118.2	118.3	118.7
A(18,20,23)	129.7	130.7	132.0	132.0	128.1
A(19,22,21)	128.3	128.3	128.6	128.4	128.4
A(22, 19, 15)	115.7	115.7	115.3	115.5	115.0
A(22,21,18)	117.5	117.6	117.2	117.4	116.7
A(24,23,28)	119.3	119.1	119.1	119.1	119.7
Dihedral angle (°)					
D(34.7.8.35)	-179.9	-180.0	180.0	-180.0	-177.3
D(5,7,8,9)	180.0	180.0	-180.0	180.0	-179.8
D(7.8.9.11)	0.0	0.0	0.0	0.0	-0.3
D(4.5.7.34)	-179.4	-179.9	-180.0	-180.0	-159.3
D(32.4.5.7)	0.1	0.0	0.0	0.0	3.0
D(8.9.10.12)	-179.8	-179.9	-180.0	-180.0	-178.2
D(11,9,10.12)	0.2	0.1	0.0	0.0	2.3
D(10,12.13.37)	-0.3	-0.2	0.0	0.0	15
D(20,18.21.22)	178.7	178.9	180.0	-180.0	178 3
D(21,18,20.23)	-2.7	-2.1	0.0	0.0	-4.1
D(38,14,12,10)	0.1	0.1	0.0	0.0	_1 4
D(40,20,23,24)	-158.1	-165.4	-180.0	180.0	-164.7

TABLE 2	Mulliken Atomic Charges (e) of (E)-3-Ph	envl-N-[4-(Phenvl-Amino) Quinazoline-7-vl] Acrvlamide
		•••••••••••••••••••••••••••••••••••••••	

Atoms	HF/6-31G*	HF/6-311G**	B3LYP/6-31G*	B3LYP/6-311G**	MP2/6-31G*
C1	-0.202	-0.083	-0.131	-0.092	-0.203
C2	-0.193	-0.089	-0.123	-0.078	-0.194
C3	-0.203	-0.080	-0.131	-0.093	-0.204
C4	-0.204	-0.084	-0.171	-0.051	-0.205
C5	0.020	-0.065	0.169	-0.073	0.012
C6	-0.216	-0.080	-0.187	-0.060	-0.211
C7	-0.128	0.031	-0.153	-0.017	-0.128
C8	-0.359	-0.300	-0.229	-0.230	-0.355
C9	0.845	0.659	0.648	0.454	0.851
N10	-0.956	-0.601	-0.761	-0.476	-0.954
011	-0.624	-0.505	-0.523	-0.377	-0.649
C12	0.401	0.284	0.385	0.207	0.401
C13	-0.245	-0.110	-0.160	-0.088	-0.252
C14	-0.301	-0.126	-0.251	-0.070	-0.302
C15	0.288	0.187	0.245	0.074	0.295
C16	-0.116	-0.212	0.117	-0.161	-0.108
C17	-0.184	-0.030	-0.223	-0.047	-0.190
C18	0.744	0.695	0.537	0.516	0.719
N19	-0.606	-0.490	-0.502	-0.346	-0.612
N20	-0.953	-0.615	-0.782	-0.482	-0.936
N21	-0.664	-0.550	-0.518	-0.406	-0.663
C22	0.282	0.265	0.171	0.138	0.285
C23	0.364	0.244	0.366	0.176	0.361
C24	-0.202	-0.095	-0.147	-0.070	-0.203
C25	-0.198	-0.079	-0.145	-0.102	-0.197
C26	-0.212	-0.116	-0.128	-0.090	-0.215
C27	-0.191	-0.076	-0.131	-0.097	-0.190
C28	-0.263	-0.158	-0.209	-0.131	-0.266
H29	0 211	0 104	0 139	0 101	0 211
H30	0.210	0 105	0.138	0 101	0.212
H31	0.209	0 102	0.138	0.099	0.210
H32	0.205	0.093	0.130	0.090	0.210
H33	0.207	0.099	0.142	0.098	0.218
H34	0.250	0.134	0.171	0 119	0.255
H35	0.193	0.093	0.127	0.090	0.197
H36	0.402	0.055	0.338	0.232	0.406
H37	0.402	0.244	0.350	0.232	0.400
1120	0.200	0.100	0.133	0.092	0.251
1120	0.218	0.090	0.137	0.092	0.213
1139	0.207	0.001	0.125	0.075	0.213
H40	0.407	0.245	0.340	0.235	0.404
	0.207	0.102	0.145	0.104	0.212
L/12	0.245	0.140	0.100	0.100	0.232
	0.204	0.100	0.152	0.030	0.204
L / 5	0.201	0.090	0.127	0.032	0.200
П4Э ЦИС	0.203	0.096	0.130	0.025	0.204
H40	0.196	0.086	0.120	0.083	0.195

 $1083 \,\mathrm{cm}^{-1}$ are assigned to C–H in-plane bending vibrations. All these bands are in the expected range.

The highly informative C–H out-of-plane bending vibrations are strongly coupled vibrations and

appear in the region 900–667 cm^{-1,[25,26]} Substitution patterns on the ring can be judged from these bands. The pure out-of-plane vibrations have shown as two absorptions at 695 cm⁻¹ and 750 cm⁻¹.

HF			B3LYP					
		6 21	C *				MP2	
No.	Freq. ^a	Unscaled	Scaled ^b	6-311G** Scaled ^c	6-31G [*] Scaled ^d	6-311G** Scaled ^e	6-31G* Scaled ^f	Assignments ^g
1		325	291	292	287	289	290	β ζ=Ο
2		448	401	400	397	399	372	ν N(20)-H
3		496	444	449	460	462	416	ν N(20)-H
4		538	482	485	479	479	444	γ C-H I. γ N(10)-H
5	511w	576	516	516	517	520	461	ν N(10)-H
6	_	597	534	534	545	539	494	ν N(10)-H
7	_	635	569	573	569	574	499	v C(5)-C(7)
8	598w	678	607	612	609	614	524	δ -Ph III
9		679	608	613	609	615	559	δ -Ph I
10		768	688	692	677	683	639	ν C-H III
11	695w	795	712	719	705	710	656	ν C-H I
12	750 m	842	754	760	740	742	686	у С-Н Ш
13		860	770	776	749	754	687	ν C-H I
14		877	785	793	783	787	759	γ C-H II Oring γ C=C
15		906	811	811	792	801	764	v C(23)-N(20) + C(24) = C(25)
16		940	842	844	819	822	779	v C-H III
17		950	851	854	832	837	786	v C-H I
18		978	876	881	836	845	798	γ -C=CH
10		989	885	888	857	865	807	y -C-CH
20	88714/	999	807	902	878	887	813	Oring trigonal breathing
20	007 W	1023	054 016	902	800	897	825	
21		1025	910	920	890	901	820	Ph II trigonal breathing
22		1032	924	920	025	901	029	
23		1045	950	939	925	929	039 QAD	Ph III trigonal broathing
24		1009	975	978	020	941	04Z 046	Ph I trigonal breathing
25		1090	970	980	021	942	040 047	
20		1094	00/	907	951	950	047 070	
27	_	1099	904 005	907	951	959	0/2	γ C(13)-Π, γ C(17)-Π
20	_	1100	905	994	959	975	904	$\gamma C = 1$
29	_	1109	995 1002	997 1006	900	975	920	V C(0) - C(9), V C(9) - N(10)
50 51	_	1120	1005	1000	970	901	951	γ C-H III
3 I 2 2	_	1127	1009	1012	977	983	964	γ C-Π I
3Z	00/11	1129	1011	1014	991	990	909	
33 24	994W	1131	1013	1016	997	997	984	
34 25		1133	1014	1021	1017	1017	1009	
35		1145	1025	1025	1018	1018	1010	
36		1166	1044	1045	1054	1054	1042	β C-H II, Q ring β C-H
3/		1190	1065	1064	1072	1071	1064	
38	1083W	1194	1069	1071	1076	1074	1069	
39	_	1213	1086	1081	1113	1110	1107	β C(25)-H, β C(26)-H
40	_	1221	1093	1089	1136	1131	1141	β C(1)-H, β C(2)-H
41	_	1274	1141	1140	1149	1147	1149	β C(13)-H, β C(14)-H
42		1295	1159	1160	1166	1163	1164	β C(13)-H, β C(17)-H
43		1305	1168	1169	1169	1165	1166	β C-H III
44		1306	1169	1170	1170	1167	1166	β C-H I
45		1315	1177	1178	1192	1189	1187	β C(1)-H, β C(2)-H
46		1320	1182	1180	1199	1195	1193	β C-H III
47	1248ms	1350	1209	1209	1230	1224	1228	β C-H I, β C(14)-H
48	—	1384	1239	1243	1280	1278	1271	ν C(23)-N(20), β C-H III

TABLE 3 Experimental and Calculated Frequencies (cm⁻¹) with General Mode Assignments for (E)-3-Phenyl-N-[4-(Phenyl-Amino) Quinazoline-7-yl] Acrylamide

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(Continued)

		HF			B3LYP		MP2	
No.	Freq. ^a	6-31 Unscaled	G [*] Scaled ^b	6-311G** Scaled ^c	6-31G* Scaled ^d	6-311G** Scaled ^e	6-31G* Scaled ^f	Assignments ^g
49		1434	1284	1285	1301	1294	1292	<i>в</i> С-Н II
50	_	1442	1291	1292	1307	1301	1302	β C(7)-H
51	_	1471	1317	1320	1317	1311	1311	ν C(22)-N(21). β C(22)-H
52	_	1484	1329	1330	1322	1318	1336	β C-H III
53		1491	1335	1335	1323	1320	1375	β C-H I
54		1498	1341	1341	1336	1329	1387	β C(8)-H
55	1369ms	1534	1373	1376	1381	1378	1397	Ph II skeleton vibration
56	1401s	1552	1390	1393	1388	1381	1406	Qring skeleton vibration
57	1443vs	1611	1442	1443	1435	1431	1424	Ph III skeleton vibration
58	_	1617	1448	1447	1440	1435	1425	Ph I skeleton vibration
59	1499vs	1664	1490	1493	1480	1477	1468	Ph II skeleton vibration
60	_	1672	1497	1497	1486	1478	1470	Ph I skeleton vibration
61	_	1674	1499	1499	1487	1479	1475	Ph III skeleton vibration
62	_	1725	1544	1550	1515	1508	1493	ν C(18)-N(20), β N(20)-H
63	1524vs	1739	1557	1559	1529	1524	1519	β N(10)-H
64	1555vs	1781	1595	1599	1570	1566	1555	Ph II skeleton vibration, β N(10)-H
65	_	1799	1611	1615	1571	1567	1559	Ph III skeleton vibration, β N(20)-H
66	_	1808	1619	1622	1596	1590	1581	Ph I skeleton vibration
67	_	1812	1621	1625	1600	1594	1582	Ph III skeleton vibration
68	1599vs	1822	1631	1636	1601	1595	1586	Ph II skeleton vibration
69	1630vs	1857	1663	1665	1627	1623	1628	v C=C
70	1670ms	1955	1750	1752	1702	1696	1680	v C=O
71	_	3345	3044	3009	3029	3012	3002	v C(24)-H
72	3030ms	3359	3057	3022	3039	3016	3003	v С-Н I, v -С=СН
73	_	3372	3069	3032	3051	3031	3018	<i>v</i> C(17)-H
74	3056ms	3376	3072	3037	3056	3036	3019	v C-H I, v -C=CH
75	_	3377	3073	3038	3062	3042	3022	v C(14)-H
76	_	3378	3074	3039	3063	3043	3027	<i>v</i> C(22)-H
77	_	3389	3084	3049	3076	3057	3043	v C-H III
78	_	3395	3089	3056	3080	3060	3044	v C-H I
79	_	3458	3147	3122	3141	3113	3092	v C(24)-H
80	_	3475	3162	3124	3142	3114	3096	v C(13)-H
81	3367ms	3880	3531	3530	3452	3462	3391	v N-H amide
82	3455ms	3919	3566	3567	3485	3492	3407	v N-H

^avs: very strong; s: strong; ms: medium strong; m: medium; w: weak.

^bWith the scale factor of 0.910 for calculated wavenumbers greater than 3000 cm^{-1} and the scale factor of 0.8953 for lower wavenumbers. ^cWith the scale factor of 0.910 for calculated wavenumbers greater than 3000 cm^{-1} and the scale factor of 0.9051 for lower wavenumbers. ^dWith the scale factor of 0.958 for calculated wavenumbers greater than 3000 cm^{-1} and the scale factor of 0.9613 for lower wavenumbers. ^eWith the scale factor of 0.958 for calculated wavenumbers greater than 3000 cm^{-1} and the scale factor of 0.9682 for lower wavenumbers. ^eWith the scale factor of 0.958 for calculated wavenumbers greater than 3000 cm^{-1} and the scale factor of 0.9682 for lower wavenumbers. ^fWith the scale factor of 0.937 for calculated wavenumbers greater than 3000 cm^{-1} and the scale factor of 0.9441 for lower wavenumbers. ^gv: stretching; β : in-plane bending; γ : out-of-plane bending; δ : deformation.

Vibration Modes of C(7) = c(8)

The characteristic C=C stretching vibration of *trans*olefin is expected to appear at about 1660 cm^{-1} . Consequently, the very strong IR band observed at 1630 cm^{-1} is attributed to the C=C stretching mode.

Amide Group Vibrations

Secondary amide shows only one N-H stretching band between 3370 and 3170 cm^{-1} in the infrared spectrum. Owing to Fermi resonance of 1550 cm^{-1} , a weaker band may appear at about 3100 cm^{-1} in secondary amides. The precise location of this



FIGURE 3 The calculated and experimental IR spectra of (E)-3--phenyl-N-[4-(phenyl-amino) quinazoline-7-yl] acrylamide. (color figure available online.)

vibration mode depends on the other groups adjacent to the -CONH- skeleton.^[27] Hence, the medium strong band observed at 3367 cm⁻¹ in IR is assigned to the N-H stretching.

There is competition for the lone pair of electrons of the nitrogen between the C=O and the phenyl ring in the title molecule. The medium strong IR band observed at 1670 cm⁻¹ is ascribed to the amide-I band, C=O stretching mode. We can see clearly from Fig. 2 that there is a bond critical point between O(11) and H(37), with $\rho(\mathbf{r})$ being 0.019 and $\nabla^2 \rho(\mathbf{r})$ being -0.017. The resulting $O(11) \cdots H(37)$ intramolecular interaction will influence the infrared frequency. Together with the conjugation of the adjacent C=C group, the O(11) \cdots H(37) weak intramolecular interaction makes the electron density of carbonyl averaged, leading to a decline in force constant of the C=O bond. As a result, the C=O bond is slightly elongated. Finally, the absorption frequency shifts to a lower wavenumber.

The peak at 1524 cm^{-1} with very strong intensity in IR is attributed to the amide-II band, N–H in-plane bending mode. The N–H out-of-plane bending is observed as a weak band at 511 cm^{-1} .

Ring Vibrations

Ring stretching vibrations are expected to occur in the range $1000-1590 \text{ cm}^{-1}$. The bands with variable intensities observed at 1369, 1401, 1443, 1499, and 1599 cm^{-1} are assigned to ring stretching vibrations. All bands appeared in the expected range. Moreover, the very strong absorption at 1555 cm^{-1} is assigned to skeleton vibration of the phenyl ring II being weakly coupled to N–H in-plane bending.

The frequencies occurring at 1000 cm^{-1} are normally assigned as the trigonal ring breathing vibration.^[28] The weak IR band occurred at 887 cm⁻¹ and is ascribed to trigonal breathing of the quinazoline ring. The ring deformation vibrations were observed at 598 cm⁻¹.

Comparisons of the Experimental and Theoretical Frequencies

Owing to the neglect of electron correlation effects and basis set deficiencies, the calculated frequencies are usually higher than the corresponding



FIGURE 4 Correlation graphs between the experimental and the theoretical wavenumbers. (color figure available online.)

TABLE 4 C	orrelation Equations	Between the 1	Theoretical and t	the Experimental	Absorption Freq	uencies
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Calculation method	Correlation equations	n	R ²	SE
HF/6-31G*	y = 1.034x - 28.913	21	0.9987	33.3
HF/6-311G**	y = 1.0259x - 16.764	21	0.9981	40.1
B3LYP/6-31G*	y = 1.0139x - 15.772	21	0.9996	19.1
B3LYP/6-311G**	y = 1.011x - 13.575	21	0.9993	24.9
MP2/6-31G*	y = 1.0093x - 36.605	21	0.9990	29.2

experimental quantities. Frequency overestimation has been reported in several papers.^[29,30] In order to fit the calculated values with the experimental ones, it is necessary to scale down the calculated harmonic frequencies. Palafox et al.^[31] described the importance of quantum chemical scaling in the calculation of the harmonic vibrational wavenumbers. The scaling factors recommended by Merrick et al.^[32] are used in this work. The unscaled and scaled wavenumbers are also reported in Table 3. After applying the scaling factors, the theoretical calculations are in good agreement with the experimental data. For visual comparison, the calculated IR spectra are also shown in Fig. 3. By plotting the computed versus the observed frequencies, the linearity between them can be judged. The correlation graph between the experimental and the theoretical wavenumbers is adopted to vividly display the agreement of the predictions with the observation (Fig. 4). The correlation equations with sample number nbeing 21 are summarized in Table 4. Generally, there are good linearity relationships between the calculated and experimental frequencies because all the correlation coefficients are larger than 0.99. On the one hand, DFT calculations, compared with the HF and MP2 methods, gave values closer to the experimental wavenumbers, since the correlation equations possessing relatively lager R^2 values and smaller SE values are the two obtained at the B3LYP/6-31G* and B3LYP/ 6-311G^{**} levels, with R^2 being 0.9996 and 0.9993, respectively, and SE being 19.1 and 24.9, respectively. The superiority of the DFT method is reflected in this aspect. On the other hand, the larger basis set does not show evident improvement in the accuracy of the vibration frequencies.

CONCLUSION

Both experimental and theoretical studies on the vibrational spectrum of (E)-3-phenyl-N-[4-(phenyl-amino) quinazoline-7-yl] acrylamide were carried

out. The molecular geometry and the wavenumbers were calculated using HF, B3LYP, and MP2 methods with the Gaussian 03 software. The scaled theoretical vibration frequencies are in excellent agreement with the experimental data. And frequencies calculated by the DFT/B3LYP method are more consistent with the experimental values than the HF method. The larger correlation coefficients ($R^2 > 0.99$) indicate that the observed frequencies may be reproduced by the computed values.

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