

Synthesis, infrared spectral studies and theoretical calculations of 4-phenyl-4,5-dihydrobenzo[*f*][1,4]oxazepin-3(2*H*)-one (thione)

Hikmet Agirbas^{a,*}, Seda Sagdinc^b, Fatma Kandemirli^a, Berat Kemal^a

^a Department of Chemistry, Kocaeli University, 41300 Izmit, Turkey

^b Department of Physics, Kocaeli University, 41300 Izmit, Turkey

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ABSTRACT

Salicylaldehyde (**1**) was reacted with aniline to afford 2-[(*E*)-(phenylimino)methyl]phenol (**2**). The reduction of (**2**) by NaBH₄ gave 2-((phenylamino)methyl)phenol (**3**) which was reacted with chloroacetyl chloride to give 2-chloro-*N*-(2-hydroxybenzyl)-*N*-phenylacetamide (**4**). Compound (**4**) was cyclized to 4-phenyl-4,5-dihydrobenzo[*f*][1,4]oxazepin-3(2*H*)-one (**5**) by NaOH in ethanol solution. The treatment of compound (**5**) with P₂S₅ gave corresponding 4-phenyl-4,5-dihydrobenzo[*f*][1,4]oxazepin-3(2*H*)-thione (**6**). The structures of (**5**) and (**6**) were determined by ¹H NMR and IR spectra. The optimized structural parameters and vibrational frequencies of (**5**) and (**6**) were calculated by DFT with 6-31G(d,p) basis set. The mechanism of the cyclization reaction was studied by RHF with the standard 3-21G basis set.

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1. Introduction

Benzoxazepines have a wide range of biological activities. The application of benzoxazepine and its derivatives is found in the research areas as having hypnotic muscle relaxation [1], antiemetic, antagonistic [2] and anti-inflammatory [3] effects. These compounds are also used as anxiolytics [4] antiallergic and antihistaminic agents [5]. The benzoxazepines with carbonyl groups have shown anxiolytic [6], central depressant [7], analgesic [8], local anesthetic [9], anti-inflammatory [10], and antihistaminic [11] effects. Additionally, benzoxazepines have also shown the stabilizing property in photography [12].

In this study, we have synthesized 4-phenyl-4,5-dihydrobenzo[*f*][1,4]oxazepin-3(2*H*)-one (**5**) and 4-phenyl-4,5-dihydrobenzo[*f*][1,4]oxazepin-3(2*H*)-thione (**6**) (Scheme 1) and report the complete assignments of their IR spectra.

With the recent advances in computer, chemical properties of small molecules can be described correctly [13–15]. Raw frequency values computed at the Hartree–Fock level contain systematic errors due to the neglect of electron correlation, resulting overestimates of about 10–12% [15]. Therefore, we selected density functional theory (DFT)(B3LYP/6-31G(d,p)) method for the vibrational frequency calculations of compounds (**5**) and (**6**).

We also report here the *ab initio* (RHF/3-21G) calculations for the cyclization of 2-chloro-*N*-(2-hydroxybenzyl)-*N*-phenylacetamide

(**4**) to obtain 4-phenyl-4,5-dihydrobenzo[*f*][1,4] oxazepin-3(2*H*)-one (**5**). The electronic structures of the reactants, their transition states, intermediate states and final products of the cyclization reaction were investigated.

2. Synthesis

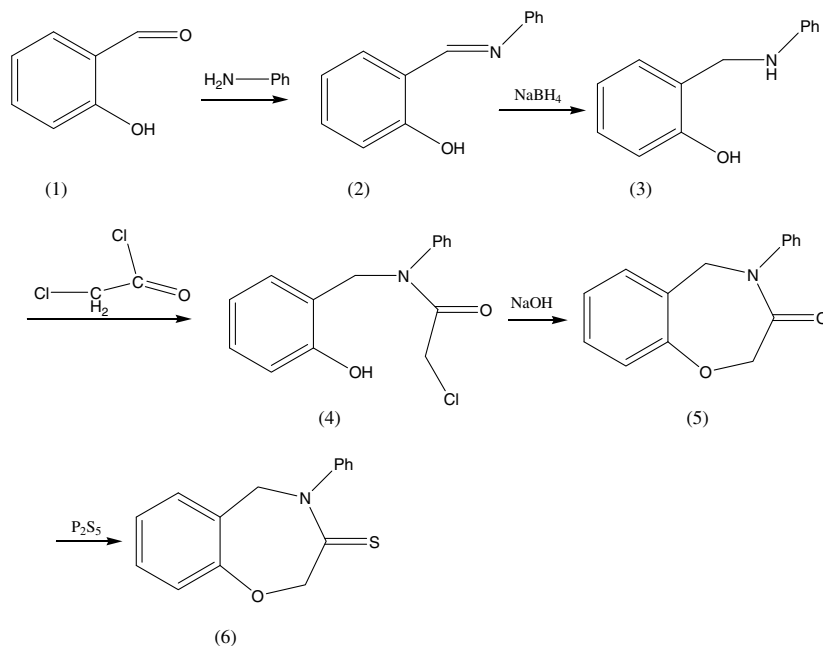
Compounds (**2–6**) were synthesized as illustrated in Scheme 1. Salicylaldehyde (**1**) was reacted with aniline to afford 2-[(*E*)-(phenylimino) methyl]phenol (**2**). Then the imine (**2**) was reduced by NaBH₄ to give 2-((phenylamino)methyl)phenol (**3**). Compound (**3**) was reacted with chloroacetyl chloride to have the corresponding amide (**4**). The cyclic ether, 4-phenyl-4,5-dihydrobenzo[*f*][1,4]oxazepin-3(2*H*)-one (**5**) was obtained in quantitative yield under the basic treatment of (**4**). Compound (**5**) was treated with P₂S₅ to give corresponding 4-phenyl-4,5-dihydrobenzo[*f*][1,4]oxazepin-3(2*H*)-thione (**6**). The compounds (**3–6**) were identified by their IR and ¹H NMR spectra.

3. Experimental

Melting points were determined in open capillaries in Electrothermal 9200 apparatus and are uncorrected. The FTIR spectra were recorded on Shimadzu 8201 spectrometer with KBr technique, in the region of 4000–400 cm⁻¹ that was calibrated by polystyrene. ¹H NMR spectra were recorded on Bruker DPX-400 (400 MHz) High Performance Digital FT-NMR Spectrometer in CDCl₃ with Me₄Si as an internal standard. Silica Gel (Fluka or Merck) were used for column chromatography.

* Corresponding author.

E-mail address: agirbas@kou.edu.tr (H. Agirbas).



Scheme 1. Synthesis of 4-phenyl-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (**5**) and 4-phenyl-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-thione (**6**).

Schiff base (**2**) (Scheme 1) was synthesized according to the literature [16]. A band for the azomethine group was observed in IR spectrum at about 1620 cm⁻¹. For the synthesis of compounds (**3–5**), literature methods [17,18] were applied with slight modifications.

3.1. Calculation methods

3.1.1. Calculation methods for IR studies

The geometries were first determined at the B3LYP exchange-correlation functional [19,20] with 3-21G basis set using HyperChem package [21]. All other calculations were then performed using Gaussian 03W program package [15], utilizing gradient geometry optimization [22]. Calculations on the molecules by this program were carried out on the basis of B3LYP exchange-correlation functional with 6-31G(d,p) basis set.

Vibrational frequencies, calculated at B3LYP/6-31G(d,p) level scaled by 0.96 [23]. All the calculations have been carried out with the restricted closed-shell formalism.

3.1.2. Calculation methods for the cyclization reaction

The calculations were performed by using the Gaussian03 Revision-B.04s by means of RHF with the standard 3-21G basis set. Natural bond analysis (NBO) (RHF/3-21G) was carried out only for chloroacetyl chloride and 2-((Phenylamino)methyl) phenol to determine the reacting atoms in the molecules.

4. Results and discussion

4.1. Geometrical parameters

The optimized structure parameters of compounds (**5**) and (**6**) were calculated by DFT with 6-31G(d,p) basis set (Table 1). The compounds consist of benzene ring (Ring₁), oxazepine ring (Ring₂) and phenyl ring (Ring₃), as seen in Fig. 1.

The calculated bond lengths of (**5**) are longer than bond lengths of (**6**) (except C(14)–N(13) bond length), because of the replace-

Table 1

Selected optimized geometrical parameters (bond length (Å), bond angles (°), dihedral angles (°)) of compounds (**5**) and (**6**)

Compounds	(5)	(6)	(5)	(6)
<i>Bond length (Å)</i>		<i>Bond angles (°)</i>		
C(6)–C(7)	1.392	1.392	C(6)–C(8)–C(12)	118.87
C(6)–C(8)	1.403	1.402	C(9)–C(8)–C(12)	123.28
C(7)–C(11)	1.396	1.396	C(8)–C(12)–N(13)	115.58
C(8)–C(9)	1.407	1.407	C(12)–N(13)–C(14)	119.32
C(8)–C(12)	1.517	1.517	C(12)–N(13)–C(17)	118.87
C(9)–O(15)	1.371	1.370	N(13)–C(17)–C(5)	121.36
C(9)–C(10)	1.401	1.401	N(13)–C(17)–C(1)	119.08
C(10)–C(11)	1.390	1.390	N(13)–C(14)–C(18)	115.10
C(12)–N(13)	1.476	1.480	N(13)–C(14)–O(16)	112.75
N(13)–C(17)	1.433	1.442	N(13)–C(14)–S(16)	–
C(14)–O(16)	1.222	–	C(14)–C(18)–O(15)	125.37
C(14)–S(16)	–	1.663	O(15)–C(9)–C(8)	114.34
C(14)–N(13)	1.380	1.356	O(15)–C(9)–C(10)	124.51
O(15)–C(18)	1.428	1.430	O(16)–C(14)–N(13)	120.36
			S(16)–C(14)–N(13)	–
			O(16)–C(14)–C(18)	120.21
			C(2)–C(1)–C(17)	120.56
			C(18)–O(15)–C(9)	120.87

ment of oxygen O(16) atom by sulfur S(16) atom. The C(14)–O(16) and C(14)–S(16) bond lengths are found 1.222 and 1.663, respectively. Calculated bond length of C(14)–S(16) is in agreement with reported value of 1.668 [24].

The energies and the dipole moments of (**5**) and (**6**) are given in Table 2.

The energy values of these two molecules were found to be –784.64 and –1107.59 au, respectively. According to this result, molecule (**6**) is more stable than molecule (**5**).

Mulliken atomic charges of C, O, N, and S atoms of molecules (**5**) and (**6**) are also given in Table 2. The N(13), O(15), C(12), O(16), and S(16) atoms, which exhibit a substantial negative charges, are the donor atoms in both of the molecules. C(17), C(14), and C(9) atoms which exhibit positive charges are the acceptor atoms.

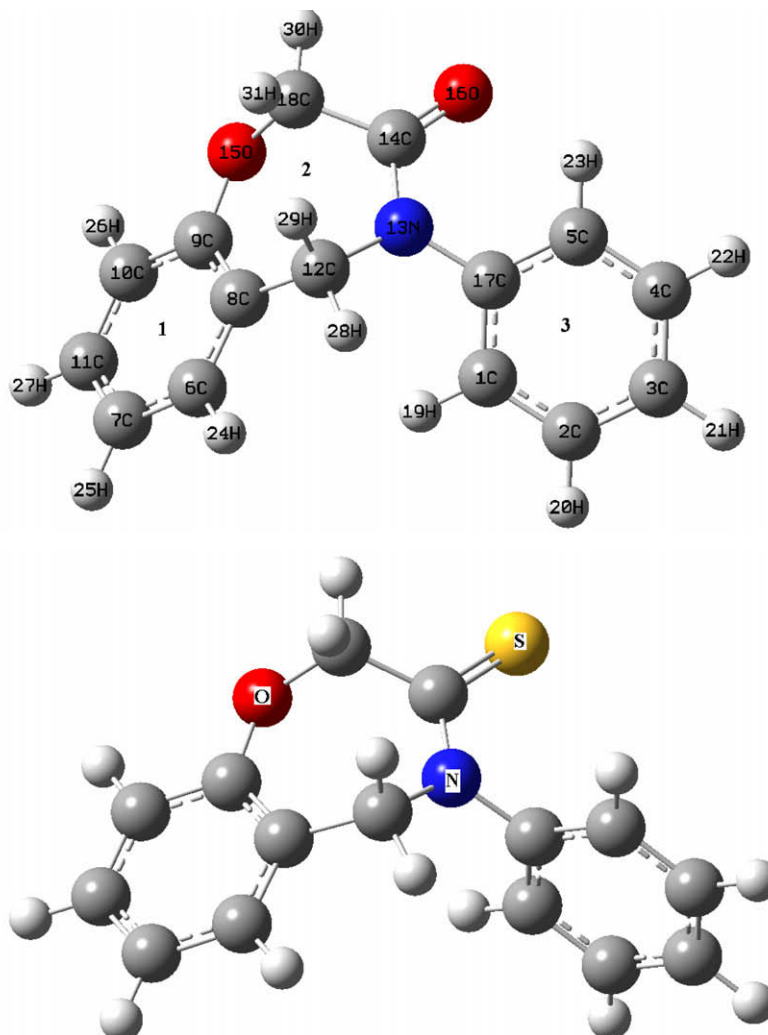


Fig. 1. Optimized geometries of compounds (5) and (6) calculated with DFT (B3LYP/6-31G(d,p)).

Table 2

The Mulliken atomic charges, dipole moments (D) and energies (a.u) obtained by B3LYP/6-31G(d,p) method

Atoms	B3LYP/6-31G(d,p)	
	Compound (5)	Compound (6)
C(1)	-0.103	-0.059
C(2)	-0.099	-0.098
C(3)	-0.078	-0.073
C(4)	-0.104	-0.097
C(5)	-0.064	-0.059
C(6)	-0.136	-0.134
C(7)	-0.087	-0.088
C(8)	0.109	0.104
C(9)	0.308	0.308
C(10)	-0.118	-0.118
C(11)	-0.087	-0.087
C(12)	-0.154	-0.138
N(13)	-0.511	-0.447
C(14)	0.552	0.131
O(15)	-0.525	-0.522
O(16)	-0.489	-
S(16)	-	-0.228
C(17)	0.250	0.205
C(18)	-0.024	0.014
Dipole moments (D)	3.5454	4.8116
Energies (a.u)	-784.64	-1107.59

4.2. FT-IR spectroscopy

The wavenumbers (in the range of 1800–400 cm^{-1}) and the intensities of the peaks in the IR spectra (Fig. 2) were compared with the calculated values (Table 3).

The correlation of calculated vibrational wavenumbers of (5) and (6) with the experimentally values gave the correlation coefficients to be 0.9993 and 0.9996, respectively (Fig. 3).

The strong and sharp band at 1661 cm^{-1} in the IR spectrum of molecule (5) was assigned as $\nu(\text{C}=\text{O})$ mode, This band was not observed in the IR spectrum of molecule (6). Dreig and Sternbach [17] reported the wavenumber of this C=O stretching band as 1675 cm^{-1} . We calculated this mode as 1743 cm^{-1} with B3LYP/6-31G(d,p) method.

The C=S group does not give a band as characteristic as the C=O group due to the complication of interactions. The C=S vibration is expected to occur at considerably lower frequencies than the C=O vibration because of the greater mass of sulfur [25]. The medium strong band observed at 1161 cm^{-1} in IR spectrum of molecule (6) was assigned as $\nu(\text{C}=\text{S})$ mode. Calculated value of this band, together with CH band (Ring₃) was found at 1159 cm^{-1} .

In the oxazine rings of both molecules, the very strong stretching $\nu_{\text{C}(14)-\text{N}(13)}$ band and the in-plane deformation $\omega_{\text{C}(14)-\text{H}(2)}$ band were observed at 1425 cm^{-1} . We have calculated

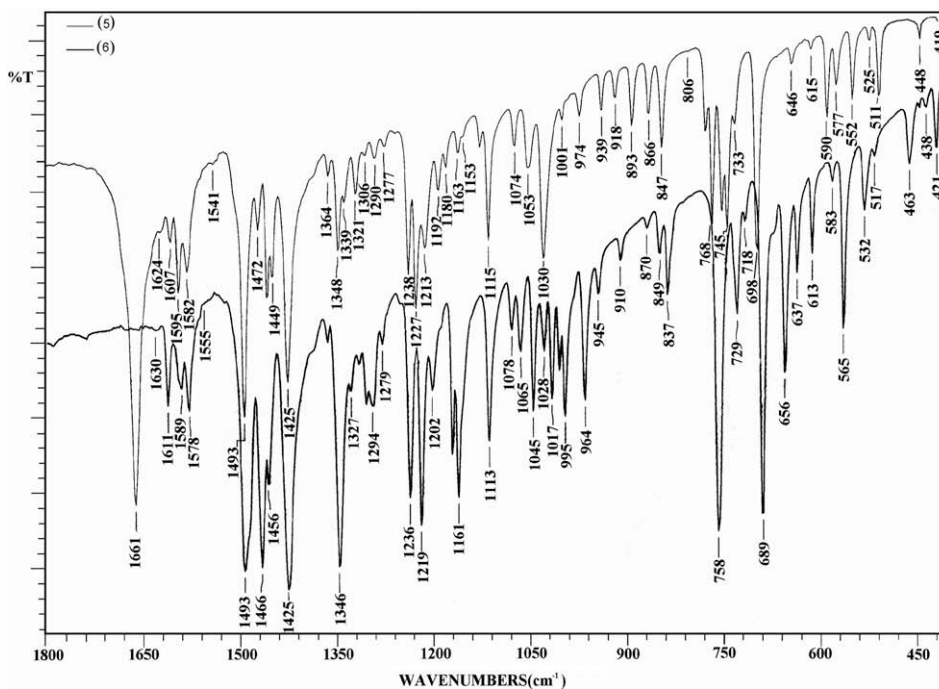


Fig. 2. A comparison of FT-IR spectra of compounds (5) and (6).

this band at 1412 cm^{-1} and 1443 cm^{-1} for molecules (5) and (6), respectively. The bands in the $1629\text{--}1493\text{ cm}^{-1}$ region were assigned as ring stretch and in-plane CH deformation modes of the molecules.

The bands at 974 cm^{-1} , 893 cm^{-1} , and 745 cm^{-1} in the IR spectrum of (5) were assigned as $\delta(\text{C}=\text{O})$ modes together with $\delta(\text{C}_{12}\text{H}_2)$, $\delta(\text{C}_{27}\text{H}_2)$ and $\delta(\text{Ring}_2)$ modes. The same bands were predicted by B3LYP/6-31G(d,p) calculations as 964 cm^{-1} , 878 cm^{-1} and 740 cm^{-1} . These bands were not observed in the IR spectrum of (6).

4.3. Calculations of the cyclization reaction

Quantum chemical calculations of the cyclization reaction have been carried out for the theoretical study on reactants, intermediates and final products. Vibrational analysis has also been performed for transition states. The stationary points were characterized by frequency calculations in order to verify that TSs had only one imaginary frequency. Intrinsic reaction coordinate (IRC) calculations have also been performed for transition states. (IRC) path was traced in order to check the energy profiles connecting each TS to the two associated minima of the proposed mechanism.

The atoms spatial arrangements in reactants, intermediates, transition states (TS) and product are shown in Fig. 4 and Fig. 5.

The charge distribution on atoms, bond lengths and bond angles of the systems participating in the reaction are given in Table 4.

The determination of reacting atoms in the reactants was done by natural bond analysis (NBO). All the other calculations for the cyclization reaction mechanism have been carried out by RHF method at the level of 3-21G basis set.

The π bonding orbital of carbonyl group in chloroacetyl chloride, **1** is polarized towards the oxygen atom. The results of NBO (RHF/3-21G) calculation yield $(0.598p)_{\text{C}25} + (0.8017p)_{\text{O}35}$. The coefficient of the carbon 2p orbital is smaller than that of oxygen.

Contrarily, π^* antibonding orbital of the same carbonyl group (Fig. 4) is polarized towards the carbon atom. The results of NBO calculation yield $(0.802p)_{\text{C}25} + (-0.598p)_{\text{O}35}$. The larger coefficient of the carbon 2p orbital means that the carbonyl π^* antibonding orbital will interact strongly to the nitrogen atom (N13) of 2-((phenylamino)methyl) phenol, **2** (Fig. 4). The orbital of lone pair electrons of nitrogen atom in 2-((phenylamino)methyl) phenol consists of 2.075% s orbital and 97, 93% p orbital. The density of electrons is $1.84e^-$.

The approach of N13 (as a nucleophile) is towards the C25 atom in a perpendicular direction to the plane of the carbonyl group. Firstly, N13 atom of molecule **1** reacts with C25 of molecule **2**. As the reacting molecules, **1 + 2** are far from each other ($\text{C}25\text{--N}13 = 2.95\text{ \AA}$), the bond lengths of $\text{C}25\text{--O}35$, $\text{C}25\text{--Cl}26$ and $\text{C}9\text{--N}13$ are 1.163 \AA , 1.954 \AA , and 1.479 \AA , respectively. The Mulliken charges of C25, N13, and O35 are 0.515 e , -0.901 e , and -0.431 e , respectively. In the first intermediate, the bond $\text{C}25\text{--N}13$ is formed. In TS1 structure, π bond is formally broken. The N13 is in a tetrahedral state, but the C25 forms a trigonal pyramid (the angles of $\text{C}9\text{--N}13\text{--H}24$, $\text{C}9\text{--N}13\text{--C}14$, $\text{C}9\text{--N}13\text{--C}25$ and $\text{N}134\text{--H}24\text{--Cl}26$ are 112.91° , 120.85° , 116.64° , 118.94°). The negative charge on N13 (-0.902 e) for **1 + 2** decreases to -0.849 e for TS1. Imaginary frequency for TS1 is -251.63 cm^{-1} . The system transition to the intermediate state **In_1** happens under the lengthen of the bond $\text{C}25\cdots\text{Cl}26$. **In_2** happens under the full breakage of the bond $\text{C}25\cdots\text{Cl}26$ and proton H24 transfer to the Cl26 atom. Imaginary frequency is -341.81 cm^{-1} for TS2. In TS3 stage, the $\text{O}11\text{--C}24$ distance becomes equal to 2.235 \AA . This stage is a cyclization stage resulting from the product **3**. In this stage full breakage of Cl26 occurs.

For reagents **1 + 2**, the total of electronic energy is $-1691,16348249\text{ au}$. For intermediates **In_1**, **In_2** and **In_3**, the totals of those are equal to $-1691,17534961\text{ au}$, $-1691,18819311\text{ au}$, and $-1232,74492990\text{ au}$, respectively. The total of the electronic energies for TS1, TS2, TS3, and TS4 are $-1691,15693545\text{ au}$, $-1691,18441118\text{ au}$, and $-1232,74241793\text{ au}$, respectively.

Table 3
Observed and calculated wavenumbers (cm^{-1}), peak intensities (km mol^{-1}) and the peak assignments of IR spectra of compounds (5) and (6)

Compounds Assignments	(5)			(6)		
	IR ^a	Calc ^b	I	IR ^a	Calc ^b	I
$\nu(\text{C}=\text{O})$	1661s	1743	283	–	–	–
$\delta(\text{CH})_{\text{Ring1}}, \nu_s(\text{Ring}_1)$	1629vw	1631	25	1624vw	1631	28
$\delta(\text{CH})_{\text{Ring3}}, \nu_s(\text{Ring}_3)$	1611w	1624	30	1606w	1622	12
$\delta(\text{CH})_{\text{Ring3}}, \nu_s(\text{Ring}_2)$	1595w	1607	3	1589vw	1610	3
$\delta(\text{CH})_{\text{Ring1}}, \nu_s(\text{Ring}_1)$	1581vw	1600	22	1578w	1601	24
$\delta(\text{CH})_{\text{Ring3}}, \nu_s(\text{Ring}_3)$	1541vw	1509	78	1554vw	1506	32
$\delta(\text{CH})_{\text{Ring1}}, \nu_s(\text{Ring}_3), \delta(\text{C}_{12}\text{H}_2)$	1493vs	1505	86	1493vs	1505	111
$\delta(\text{C}_{12}\text{H}_2), \delta(\text{C}_{18}\text{H}_2)$	1472vw	1492	9	–	1497	17
$\delta(\text{C}_{12}\text{H}_2), \delta(\text{C}_{27}\text{H}_2), \delta(\text{CH})_{\text{Ring1}}, \nu_s(\text{Ring}_1)$	1458mw	1469	19	–	1468	49
$\delta(\text{C}_{12}\text{H}_2), \nu(\text{C}_{14}\text{N}_{13})$	1449w	1468	7	1456w	1464	14
$\nu(\text{C}_{14}\text{N}_{13}), \omega(\text{C}_{14}\text{H}_2)$	1425vs	1412	161	1425vs	1443	243
$\delta(\text{C}_{14}\text{H}_2), \delta(\text{C}_{18}\text{C}_{14})$	1364vw	1366	13	1364vw	1374	2
$\nu(\text{C}_{14}\text{N}_{13}), \omega(\text{C}_{18}\text{H}_2)$	1348mw	1354	68	1346vs	1352	193
$\delta(\text{CH})_{\text{Ring3}}, \nu_s(\text{Ring}_3)$	1339vw	1337	8	–	1328	1
$\nu_s(\text{Ring}_1), \delta(\text{C}_{12}\text{H}_2), \nu_s(\text{Ring}_2)$	1321w	1324	2	1327vw	1325	26
$\delta(\text{C}_{12}\text{H}_2), \nu_s(\text{Ring}_2)$	1306vw	1319	7	1304vw	1316	5
$\delta(\text{CH})_{\text{Ring3}}, \nu_s(\text{Ring}_3)$	1290vw	1289	17	1294vw	1306	1
$\delta(\text{C}_{12}\text{H}_2), \delta(\text{C}_{18}\text{H}_2), \nu_s(\text{Ring}_1)$	1276vw	1275	24	1279vw	1286	7
$\tau(\text{C}_{18}\text{H}_2), \nu(\text{CO}_{15})$	1238m	1245	139	1236ms	1251	138
$\tau(\text{C}_{18}\text{H}_2)$	1221ms	1223	8	1219ms	1233	62
$\tau(\text{C}_{12}\text{H}_2)$	1213vw	1208	103	–	–	–
$\delta(\text{CH})_{\text{Ring1}}, \nu_s(\text{Ring}_1)$	–	–	–	1201w	1207	38
$\nu(\text{CC})_{\text{Ring2}}, \delta(\text{CH})_{\text{Ring1}}, \nu_s(\text{Ring}_1)$	1192w	1191	8	–	1192	4
$\delta(\text{CH})_{\text{Ring3}}$	1180vw	1186	3	–	1175	5
$\delta(\text{CH})_{\text{Ring3}}$	1163vw	1164	0.1	–	1164	0.02
$\nu(\text{CS}), \delta(\text{CH})_{\text{Ring3}}$	–	–	–	1161ms	1159	30
$\nu(\text{CO}), \text{Ring}_3(\text{CH})$	1135vw	1122	–	–	–	–
$\delta(\text{CH})_{\text{Ring1}}$	1115m	1118	34	–	–	–
$\nu(\text{C}_{14}\text{N}_{13}), \nu(\text{CS})$	–	–	–	1113m	1118	37
$\delta(\text{CH})_{\text{Ring3}}, \nu_a(\text{Ring}_3), \nu_a(\text{Ring}_1), \nu(\text{C}_{12}\text{N}_{13}), \delta(\text{C}_{27}\text{H}_2)$	1074w	1088	5	1078w	1082	6
$\nu_a(\text{Ring}_1), \nu(\text{C}_{12}\text{N}_{13}), \delta(\text{C}_{27}\text{H}_2)$	1053w	1055	20	1064vw	1069	5
$\nu_a(\text{Ring}_1), \nu(\text{Ring}_2), \nu_a(\text{Ring}_1), \nu(\text{C}_{27}\text{O}_{15})$	–	1039	6	1045m	1049	22
$\delta(\text{Ring}_1), \nu(\text{C}_{27}\text{O}_{15})$	1030m	1033	39	1028w	1033	10
$\delta(\text{C}_{18}\text{H}_2), \delta(\text{C}_{12}\text{H}_2), \nu(\text{Ring}_2)$	1001vw	997	0.3	1005vw	1002	14
$\delta(\text{Ring}_3)$	–	974	0.4	995m	998	7
$\delta(\text{C}=\text{O}), \delta(\text{C}_{12}\text{H}_2), \delta(\text{C}_{18}\text{H}_2)$	974m	964	11	–	–	–
$\delta(\text{C}_{18}\text{H}_2), \delta(\text{C}_{12}\text{H}_2), \delta(\text{CS})$	–	–	–	964m	957	17
$\gamma(\text{CH})_{\text{Ring3}}$	939w	952	0.4	945w	952	0.03
$\nu_a(\text{Ring}_1), \nu(\text{Ring}_2), \delta(\text{Ring}_1), \nu(\text{C}_{27}\text{O}_{15})$	–	1039	6	1045m	1049	22
$\delta(\text{Ring}_1), \nu(\text{C}_{27}\text{O}_{15})$	1030m	1033	39	1028w	1033	10
$\delta(\text{C}_{18}\text{H}_2), \delta(\text{C}_{12}\text{H}_2), \nu(\text{Ring}_2)$	1001vw	997	0.3	1005vw	1002	14
$\delta(\text{Ring}_3)$	–	974	0.4	995m	998	7
$\delta(\text{C}=\text{O}), \delta(\text{C}_{12}\text{H}_2), \delta(\text{C}_{18}\text{H}_2)$	974m	964	11	–	–	–
$\delta(\text{C}_{18}\text{H}_2), \delta(\text{C}_{12}\text{H}_2), \delta(\text{CS})$	–	–	–	964m	957	17
$\gamma(\text{CH})_{\text{Ring3}}$	939w	952	0.4	945w	952	0.03
$\gamma(\text{CH})_{\text{Ring1}}$	–	927	3	–	926	3
$\gamma(\text{CH})_{\text{Ring3}}$	918w	906	4	910w	910	0.4
$\delta(\text{C}=\text{O}), \delta(\text{Ring}_2)$	893mw	878	17	–	–	–
$\gamma(\text{CH})_{\text{Ring1}}$	870vw	856	8	866mw	861	4
$\delta(\text{Ring}_1), \delta(\text{C}_8\text{C}_{12}\text{N}_{13})$	847mw	839	5	849vw	841	7
$\gamma(\text{CH})_{\text{Ring3}}$	–	831	0.5	837mw	835	3
$\omega(\text{CH})_{\text{Ring3}}$	779w	767	11	–	770	9
$\omega(\text{CH})_{\text{Ring1}}$	768m	757	25	758vs	755	37
$\omega(\text{Ring}_2), \delta(\text{CH})_{\text{Ring3}}$	755m	752	45	–	–	–
$\text{C}=\text{O}, \omega(\text{Ring}_2)$	745m	740	14	–	–	–
Skeletal	732vw	733	4	729mw	733	2
$\delta(\text{CH})_{\text{Ring1}}$	–	–	–	717vw	724	17
$\delta(\text{Ring}_2)$	698s	698	17	689vs	695	25
CNS	–	–	–	656m	645	11
$\delta(\text{Ring}_1), \delta(\text{Ring}_2), \delta(\text{Ring}_3)$	646vw	640	1	–	–	–
CNS	–	–	–	636w	630	7
$\tau(\text{Ring}_3)$	615vw	618	1	613w	617	2
$\tau(\text{C}_{18}\text{H}_2), \tau(\text{C}_{12}\text{H}_2), \omega(\text{CO}), \delta(\text{CN})$	590mw	586	6	–	–	–
$\tau(\text{C}_{18}\text{H}_2), \tau(\text{C}_{12}\text{H}_2), \delta(\text{CS}), \delta(\text{CN})$	–	–	–	583vw	582	8
$\delta(\text{C}_{18}\text{H}_2), \delta(\text{C}_{12}\text{H}_2), \delta(\text{Ring}_3), \delta(\text{CO})$	577w	571	9	–	–	–
$\delta(\text{C}_{18}\text{H}_2), \delta(\text{C}_{12}\text{H}_2), \delta(\text{CS}), \delta(\text{CN})$	–	–	–	565m	562	12
$\delta(\text{C}=\text{O}), \delta(\text{C}_{27}\text{H}_2)$	552mw	545	10	–	–	–
$\gamma(\text{Ring}_1), \gamma(\text{Ring}_2)$	525vw	522	0.3	532w	534	2
$\gamma(\text{Ring}_1), \gamma(\text{Ring}_2), \gamma(\text{Ring}_2)$	–	–	–	517vw	513	1
$\tau(\text{Ring}_3), \tau(\text{Ring}_2), \gamma(\text{C}=\text{O})$	511mw	504	6	–	–	–
$\delta(\text{C}_{18}\text{O}_{15})$	–	461	1	463w	459	1
$\tau(\text{C}_{12}\text{H}_2)$	437vw	444	8	448vw	450	3

Vibrational modes: ν , stretching; δ , in-plane deformation; γ , out-of-plane deformation; τ , twisting; ω , wagging Superscript s, strong; m, medium; w, weak; vw, very weak.^a IR (in KBr).^b Scaled by 0.96.

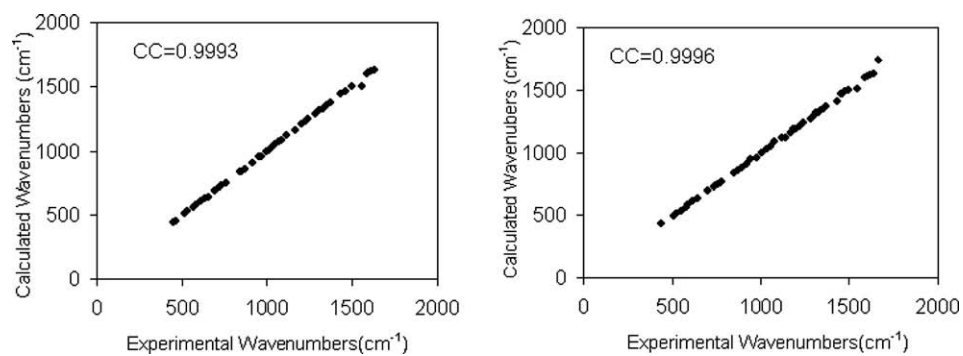


Fig. 3. Graphic correlation between the experimental and calculated wavenumbers obtained by DFT (B3LYP/6-31G(d,p)) method for compounds (5) and (6).

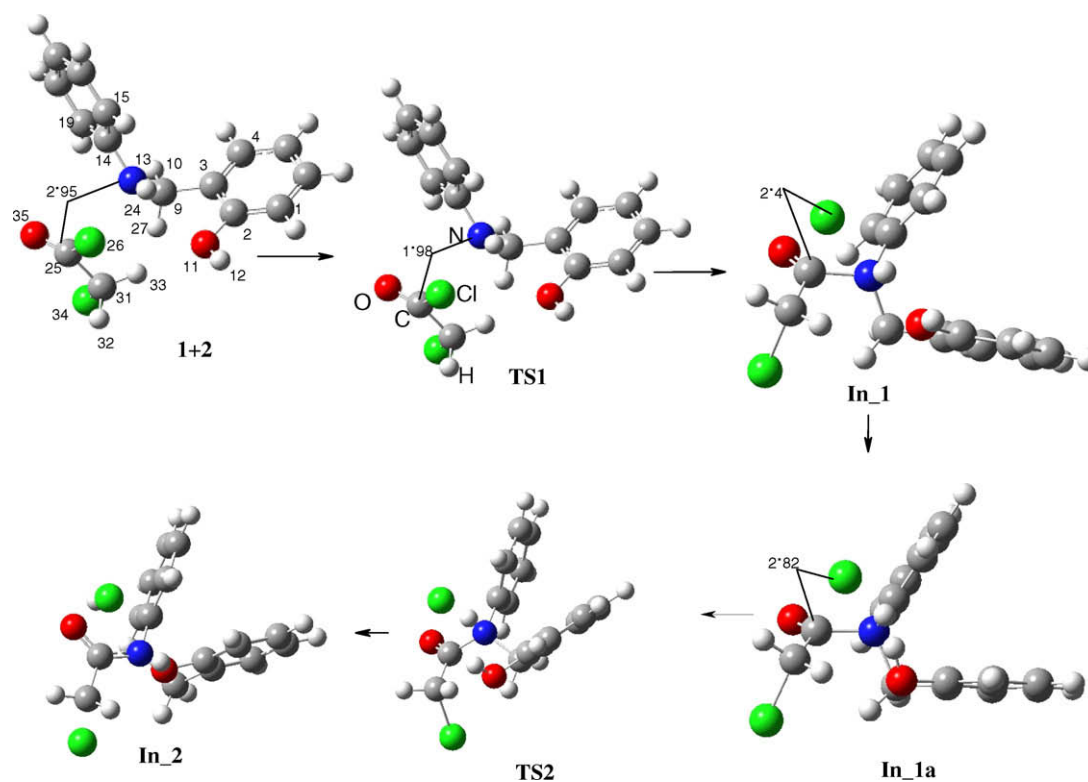


Fig. 4. Optimized forms for I+2, TS1, In_1, TS2, In_2 calculated with RHF/3-21G.

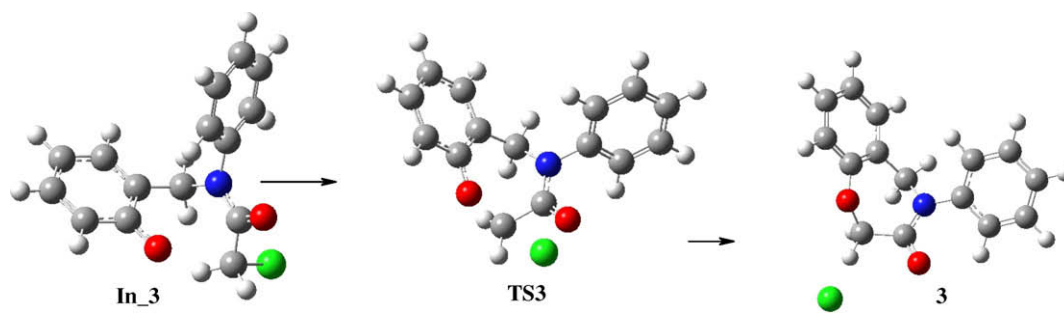


Fig. 5. Optimized forms for I+2, TS1, In_3, TS3, 3 calculated with RHF/3-21G.

Table 4
Geometric and electronic values of reactants, intermediates, transition states and product

	1+2	TS1	1n_1	1n_1a	TS2	1n_2	1n_3	TS3	3
Bond length (Å)									
C3–C9	1.516	1.513	1.504	1.501	1.502	1.513	1.505	1.516	1.518
C9–H10	1.078	1.077	1.076	1.075	1.078	1.081	1.083	1.081	1.079
C9–H27	1.080	1.075	1.074	1.074	1.072	1.075	1.078	1.082	1.082
C9–N13	1.479	1.520	1.536	1.550	1.536	1.474	1.489	1.478	1.478
N13–C14	1.407	1.450	1.476	1.477	1.472	1.438	1.430	1.377	1.415
C3–C2	1.388	1.389	1.388	1.389	1.386	1.388	1.426	1.423	1.392
C2–O11	1.391	1.386	1.384	1.385	1.385	1.382	1.282	1.291	1.368
O11–H12	0.965	0.965	0.965	0.977	0.969	0.965			
C25–N13	2.950	1.986	1.561	1.522	1.452	1.359	1.361	1.377	1.379
C31–Cl34	1.865	1.891	1.927	1.912	1.890	1.890	1.934	2.045	3.000
C31–H32	1.074	1.069	1.068	1.065	1.071	1.070	1.069	1.056	1.066
C31–H33	1.076	1.072	1.069	1.070	1.073	1.072	1.071	1.063	1.074
C31–C25	1.486	1.494	1.506	1.505	1.50826	1.515	1.510	1.509	1.520
C25–O35	1.163	1.167	1.192	1.193	1.19440	1.515	1.220	1.215	1.216
C25–Cl26	1.954	2.206	2.400	2.820	3.362	4.319			
N13–H24	1.001	1.009	1.020	1.033	1.263	3.866			
Cl26–H24	2.912	2.498	2.343	2.033	1.688	1.301			
C31–O11							2.600	2.235	1.468
Mulliken charges									
C3	-0.101	-0.114	-0.120	-0.130	-0.121	-0.098	-0.182	-0.179	-0.080
C9	-0.180	-0.219	-0.218	-0.224	-0.215	-0.151	-0.156	-0.156	-0.215
H10	0.238	0.259	0.278	0.279	0.273	0.247	0.205	0.220	0.228
H27	0.252	0.288	0.323	0.324	0.311	0.270	0.248	0.230	0.357
N13	-0.902	-0.849	-0.927	-0.952	-0.965	-0.971	-0.964	-1.003	-1.010
C14	0.344	0.259	0.272	0.258	0.250	0.303	0.317	0.372	0.383
C2	0.388	0.396	0.401	0.390	0.422	0.400	0.488	0.477	0.430
O11	-0.758	-0.759	-0.766	-0.771	-0.763	-0.774	-0.819	-0.807	-0.743
H12	0.409	0.417	0.429	0.447	0.433	0.423			
C25	0.515	0.692	0.768	0.817	0.829	0.912	0.918	0.960	0.910
C31	-0.674	-0.611	-0.566	-0.616	-0.662	-0.657	-0.588	-0.423	-0.214
H32	0.385	0.345	0.316	0.349	0.351	0.324	0.377	0.294	0.328
H33	0.328	0.354	0.366	0.366	0.344	0.315	0.281	0.321	0.260
O35	-0.431	-0.506	-0.531	-0.092	-0.497	-0.614	-0.640	-0.652	-0.639
Cl26	-0.173	-0.506	-0.708	-0.794	-0.648	-0.260	-0.217	-0.375	-0.911
Dipole moment (D)	5.75	8.27	11.317	9.18	6.18	4.73	6.24	6.62	14.04
Bond angles (°)									
C9–N13–H24	112.91	108.56		106.25		107.76	110.08		116.69
C9–N13–C14	120.85	112.96		111.51		112.43	110.53		115.96
C9–N13–C25	116.64	118.47		113.18		114.03	114.92		125.57
N13–H24–Cl26	118.94	107.30		106.66		137.10	171.45		136.08
		1n_3				TS3			3
C14–C18–O15		83.50				76.07			105.80
C14–C18–Cl32		107.84				103.55			91.05
C14–C18–H31		108.45				111.03			107.88
C14–C18–H30		113.13				121.97			115.05

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References

- [1] T. Hirohashi, T. Izumi, H. Yamamoto, Ger. Offen. 2, 014, 223(Cl. C 07d) (1970).
- [2] F. Okada, Y. Torii, H. Saito, N. Matsuki, Jpn. J. Pharmacol. 2 (64) (1994) 109.
- [3] R.A. Mueller, Ger. Offen. 2,700,091 (Cl. C07D413/12) (1977).
- [4] R.C. Effland, G.C. Helsley, J.J. Tegeler, J. Heterocyclic Chem. (1982) 537.
- [5] A.D. Cale, B.V. Franko, C.A. Leonard, Eur. Pat. Appl. EP107, 930(Cl. C07D267/14) (1984).
- [6] T. Tatsuoka, K. Nomura, M. Shibata, M. Kawai, Eur. Pat. Appl. EP 468,562 (Cl. C07D417/06) (1992).
- [7] J. Himizu, A. Ishida, K. Yoshikawa, Japan 72 48,380 (Cl. C07cd, A61k) (1970).
- [8] K. Schenker, Swiss 505, 850 (Cl. C07d) (1968).
- [9] J. Nichimizu, A. Ishida, K. Yoshikawa, T. Tokada, Japan 75 06, 531 (Cl. C07D, a61K) (1975).
- [10] D.R. Schridhar, C.R. Sarma, R.R. Krishna, Indian J. Chem. Sect. B. 17B(2)(1979) 155.
- [11] A.D. Cale, H. Robins, U.S., US 4, 705, 853 (Cl. 540-490; C07D281/08) (1987).
- [12] Y. Kaneko, Jpn. Kokai Tokyo Koho JP 63 95, 442[88 95, 442][Cl. G03C7/38] (1988).
- [13] W.J. Hehre, L. Radom, P.P.R. Schleyer, J.A. Pople, Ab Initio Molecular Orbital Theory, Wiley, New York, 1986.
- [14] J.B. Foresman, A. Frisch, Exploring Chemistry with Electronic Structure Methods, second ed., Gaussian Inc, Pittsburg, PA, 1996.
- [15] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery, Jr., T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian 03, Revision B.05, Gaussian, Inc., Wallingford CT, 2004.
- [16] A.I. Vogel, Practical Organic Chemistry, Longman, London, 1972.
- [17] M.E. Derieg, L.H. Sternbach, J. Heterocycl. Chem. 3 (1966) 237.
- [18] Y. Davion, G. Guillaumet, J.-M. Leger, C. Jarry, B. Lesur, J.-Y. Merour, Heterocycles 63 (5) (2004) 2004.
- [19] A.D. Becke, J. Chem. Phys. 98 (1993) 5648.
- [20] C. Lee, W. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785.
- [21] HyperChem 7.2 for Windows, Hypercube, Inc. USA, 2002.

- [22] H.B. Schlegel, *J. Comput. Chem.* 3 (1982) 214.
- [23] J.A. Pople, H.B. Schlegel, K. Raghavachari, D.J. Defrees, J.S. Binkley, M.J. Frisch, R.A. Whiteside, R.F. Hout, W.J. Hehre, *Int. J. Quantum Chem.* 15 (1981) 269.
- [24] Z. Li, Q.Q. Meng, Q.R. Wang, F.G. Tao, *Chinese J. Chem.* 22 (2004) 290.
- [25] N.B. Colthup, L.H. Daly, S.E. Wieberley, *Introduction to Infrared and Raman Spectroscopy*, third ed., Academic Press, 1990.