Synthesis and Characterization of New Seven-Membered Heterocyclic Compounds from Reaction of New Schiff-Bases with Maleic and Phthalic anhydrides

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Abstract

A series of new Schiff base and 1,3-Oxazepine compounds have been synthesized. 4-Aminophenazone was condensed with various aromatic aldehydes in ethanol in the presence of glacial acetic acid as catalyst to yield the Schiff base [2-4]. These Schiff bases were reacted with maleic anhydride and phthalic anhydride in dry benzene to give a seven-membered heterocyclic ring derivatives [5-7] and [8-10], respectively.

The prepared compounds were identified by their uncorrected melting points, elemental analysis and FT-IR spectra.

الخلاصة

تم تحضير عدد من قواعد شيف الجديدة ومركبات 3،1– أوكسازيبين. بتكاثف المركب 4-أمينوفينازون مع ألديهايدات مختلفة بوجود حامض الخليك الثلجي كعامل مساعد تم الحصول على قواعد شيف [2-4]. فوعلت قواعد شيف هذه مع أنهدريد الماليك وأنهدريد الفثاليك في البنزين الجاف فأعطت مشتقات سباعية الحلقة غير متجانسة [5-7] و[8-10] على التوالي.

شخصت جميع المركبات المحضرة باستخدام درجات انصهارها غير المصححة وتحليل العناصر الدقيق وأطياف الأشعة تحت الحمراء.

Introduction

Oxazepine ring is unsaturated seven-membered hetrocycle. 1,3-Oxazepine ring containing two hetero atoms are oxygen in position (1) and nitrogen in position (3) in addition of five carbon atoms. The classical methods for preparing oxazepine ring are limited [1]. Recently, cycloaddition reaction, which is a type from a pericyclic reactions is used to synthesis of 1,3-oxazepine ring [2-7]. This type of reactions is not limited and gives various1,3-oxazepine derivatives. Synthesis of these compounds in this work is a class of a pericyclic reaction which is classified as a 5+2 ⟶ 7, implying five-atom component plus two-atom component leading to seven-membered cyclic ring [8-11]. Oxazepine derivatives showed biological activities against different types of bacteria, in addition of their uses as inhibitors of some enzymes action [4,12].

The chemistry of the carbon-nitrogen double bond plays a vital role in the progresses of chemistry science [13,14]. Schiff-base compounds have been used as fine chemicals and medical substrates. Synthesis of schiff-base through classical condensation of aldehydes (or ketones) and amines were pursued [17,18]. Schiff-bases are associated with antibacterial, antifungal and antitubercular activities and have diverse biological activities [19].

In this work, we synthesized three new Schiff-base compounds and sex new 1,3-oxazepine compounds. The chemical structures of both Schiff-bases and 1,3-oxazepine compounds were studied.

Experimental

General

- All chemicals were supplied from commercial sources and used as received.
- TLC were performed on pre-coated sheets with 0.25 mm layer of Silica Gel GF254 of the Merck company, the detection was followed by coloring with iodine or H_2SO_4 in ethanol (60%) followed by heating .
- All measurements were carried out by:-
  - Melting point: Gallen kamp capillary melting point apparatus.
  - FT-IR spectra: Fourrier transform infrared Testscan Shimadzu model 8400s.
  - Elemental analysis (C. H. N.): E.A.300, Euro-Vector, Italy, 2003.

Synthesis of compounds

Synthesis of 4-[4-(dimethylamino) benzylideneamino]-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one [2]

4-(Dimethylamino)benzaldehyde (0.745g, 5mmol) containing three drops of glacial acetic acid was dissolved in absolute ethanol (15mL), then 4-Aminophenazone [1] (1.015g, 5mmol) was dissolved in absolute ethanol (15mL) and then added dropwise. The reaction mixture was refluxed with stirring on a water bath at 75ºC for 1.5h. Then the mixture was allowed to cool down at room temperature and the solvent was evaporated. The colored precipitate was filtered and washed well with cold ethanol; yield and melting point were shown in Table (I).

Synthesis of 4-(4-isopropylbenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one [3]

4-Isopropylbenzaldehyde (0.740g, 5mmol) containing three drops of glacial acetic acid was dissolved in absolute ethanol (15mL), then 4-Aminophenazone [1] (1.015g, 5mmol) was dissolved in

absolute ethanol (15mL) and then added dropwise. The reaction mixture was refluxed with stirring on a water bath at 75ºC for 4h. Then the mixture was allowed to cool down at room temperature and the solvent was evaporated. The colored precipitate was filtered and washed well with cold ethanol; yield and melting point were shown in Table (I).

Synthesis of 4-(4-bromobenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one [4]

4-Bromobenzaldehyde (0.925g, 5mmol) containing three drops of glacial acetic acid was dissolved in absolute ethanol (15mL), then 4-Aminophenazone [1] (1.015g, 5mmol) was dissolved in absolute ethanol (15mL) and then added dropwise. The reaction mixture was refluxed with stirring on a water bath at 75ºC for 1h. Then the mixture was allowed to cool down at room temperature and the solvent was evaporated. The colored precipitate was filtered and washed well with cold ethanol; yield and melting point were shown in Table (I).

Synthesis of 3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-[4-(dimethylamino)phenyl]-2,3-dihydro-1,3-oxazepine-4,7-dione [5]

Schiff base derivative [2] (0.1670g, 0.5mmol) and Maleic anhydride (0.0490g, 0.5mmol) were dissolved in (20mL) of dry benzene. The reaction mixture was refluxed with stirring at 85ºC for 5h. The mixture was then allowed to cool down at room temperature, a colored precipitate developed, filtered and recrystallized from dioxan, yield and melting point were shown in Table (I).

Synthesis of 3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-(4-isopropylphenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione [6]

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Synthesis of 2-(4-bromophenyl)-3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione [7]

Schiff base derivative [4] (0.1850g, 0.5mmol) and Maleic anhydride (0.0490g, 0.5mmol) were dissolved in (20mL) of dry benzene. The reaction mixture was refluxed with stirring at 85ºC for 5h. The mixture was then allowed to cool down at room temperature, a colored precipitate developed, filtered and recrystallized from dioxan, yield and melting point were shown in Table (I).

Synthesis of 4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3-(4-(dimethylamino)phenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione [8]

Schiff base derivative [2] (0.1670g, 0.5mmol) and Phthalic anhydride (0.0740g, 0.5mmol) were dissolved in (20mL) of dry benzene. The reaction mixture was refluxed with stirring at 85ºC for 5h. The mixture was then allowed to cool down at room temperature, a colored precipitate developed, filtered and recrystallized from dioxan, yield and melting point were shown in Table (I).

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Synthesis of 3-(4-bromophenyl)-4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione [10]

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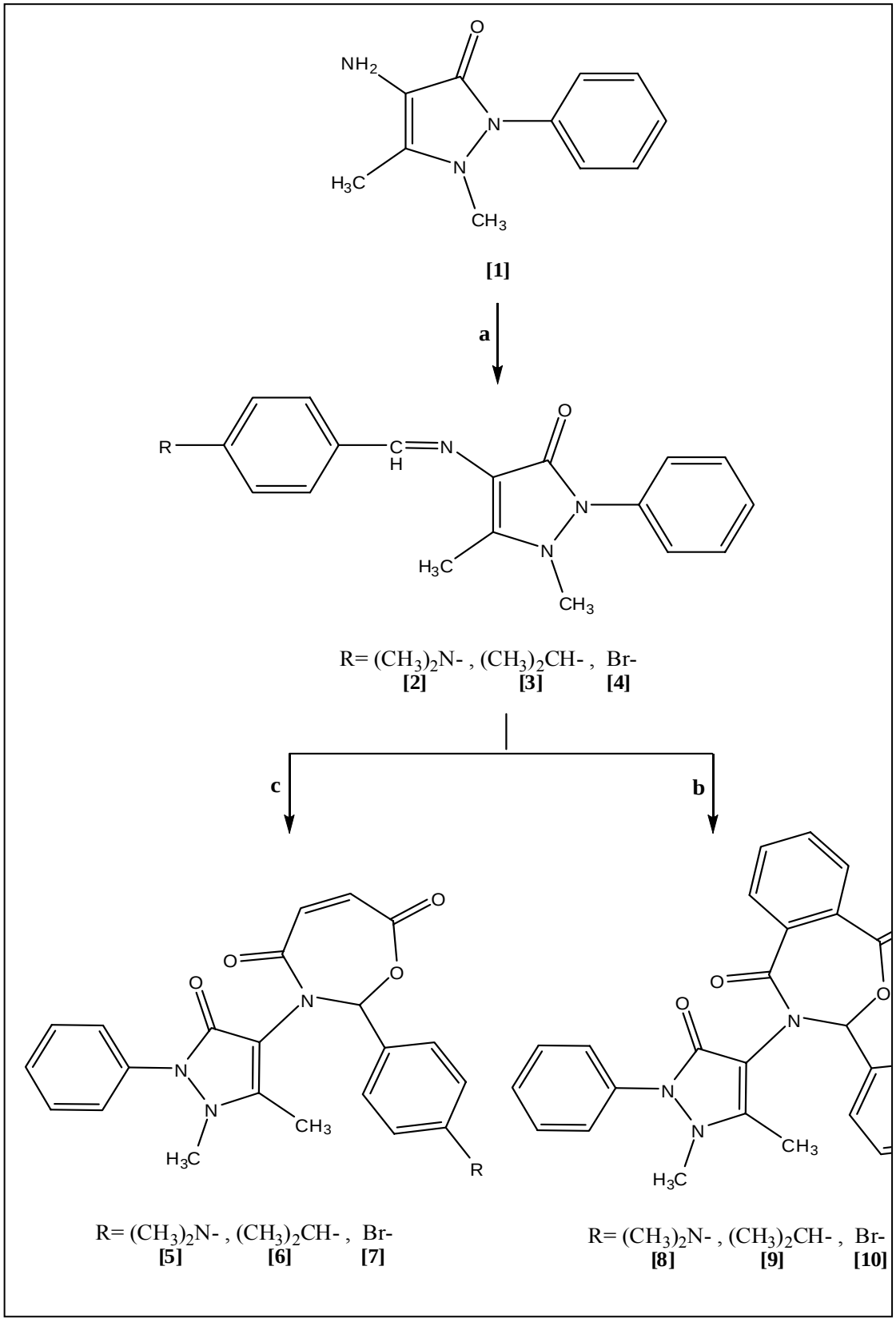
Results and Discussion

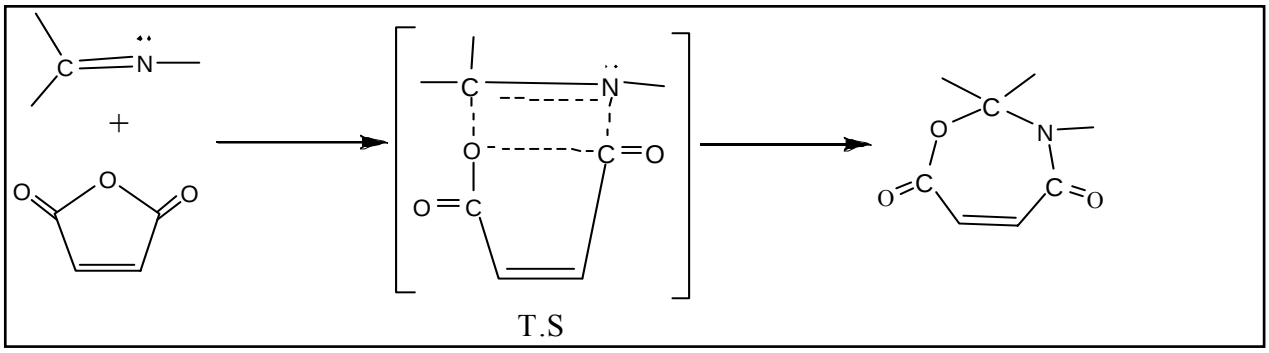
The objective of this work is the synthesis of new seven-membered heterocyclic compounds by using a pericyclic reaction between new imines with cyclic anhydrides are maleic anhydride and phthalic anhydride in dry benzene. These compounds may have biological effects besides being prepared for the first time.

First, the aromatic aldehydes were condensated with 4-aminophenazone to give Schiff-bases [2-4] according to well-known procedure [20,21]. Compounds [2], [3] and [4] were reacted [2,3,4,5,10,11] with each one of anhydrides (maleic anhydride and phthalic anhydride) to produce seven-membered heterocyclic compounds [5-10] of oxazepine as it is shown in scheme (I):



Scheme (I): a) Appropriate aldehydes, abs.Ethanol, ref. 1-4hrs b) Maleic anhydride, dry benzene, ref. 5hrs c) Phthalic anhydride, dry benzene, ref. 5hrs

Mechanism of the percyclic reaction between an imine group and maleic anhydride for preparing 1,3-oxazepine ring systematically investigated as (5+2) cycloaddition. The breaking and formation of bonds occur simultaneously and thus the reaction proceeds via a single cyclic transition state and there is no chance for formation an intermediate as it was shown in scheme (II) [10]:



Scheme (II): Approximate transition state geometry for addition of maleic anhydride to imine group

All new synthesized compounds [2-10] have been characterized by their melting points, FT-IR spectra and (C. H. N.) analysis {all results showed in Table (1) and Table (2)}. These results are compared with those obtained earlier [3,4,5]. Elementary analysis showed good agreement of the calculated and found percentages.

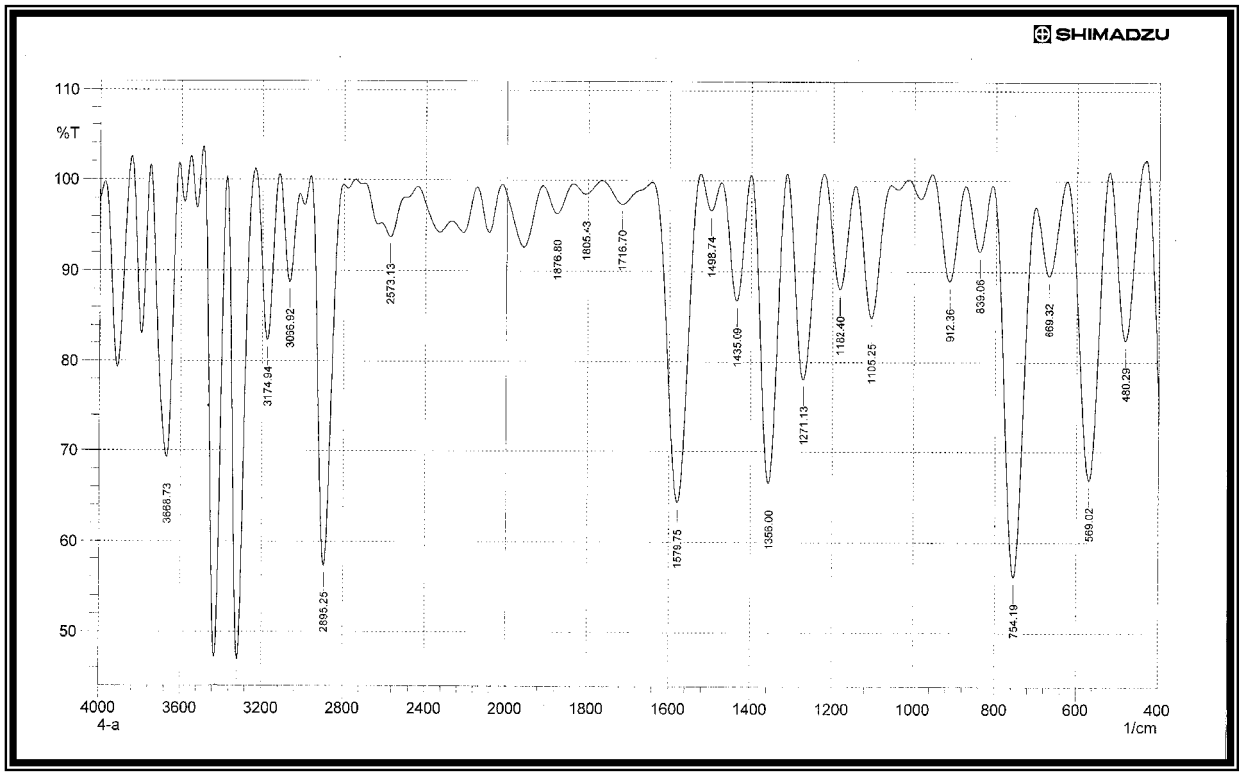
Compound [1] showed identical melting point with that published. Compound [1] was also characterized with FT-IR spectrum which showed the two bands at $3432cm^{-1}$ and $3320cm^{-1}$ were due to asymmetric and symmetric stretching vibration of ($-NH_2$) group. Moreover, FT-IR spectrum of compound [1] showed appearance of another important characteristic absorption bands shown in Table (2). FT-IR spectra of Schiff-bases derivatives [2], [3] and [4] showed disappearance of absorption bands at $3432cm^{-1}$ and $3320cm^{-1}$ attributed to the ($-NH_2$) stretching vibrations and appearance of a strong absorption bands at $1656cm^{-1}$, $1652cm^{-1}$ and $1650cm^{-1}$, respectively due to the Schiff-base group (C=N), while this bands disappear and two bands appeared at (1720-1730/1639-1676)cm^{-1} due to (lactone/lactam) groups of 1,3-oxazepine compounds [5-10]. Also, the absorption bands at (505-509)cm^{-1} were due to the presence of (C-Br) group of compounds [4], [7] and [10] [22,23,24]. This information above evidence to formation of compounds [2-10]. Other data of functional groups shown in Table (2). (C. H. N.) Analysis and melting points of compounds [1-10] shown in Table (1).

Table (I): Melting points, yield, molecular formula (M.F.), molecula weight (M.Wt.) and element analysis of compounds [1-10]

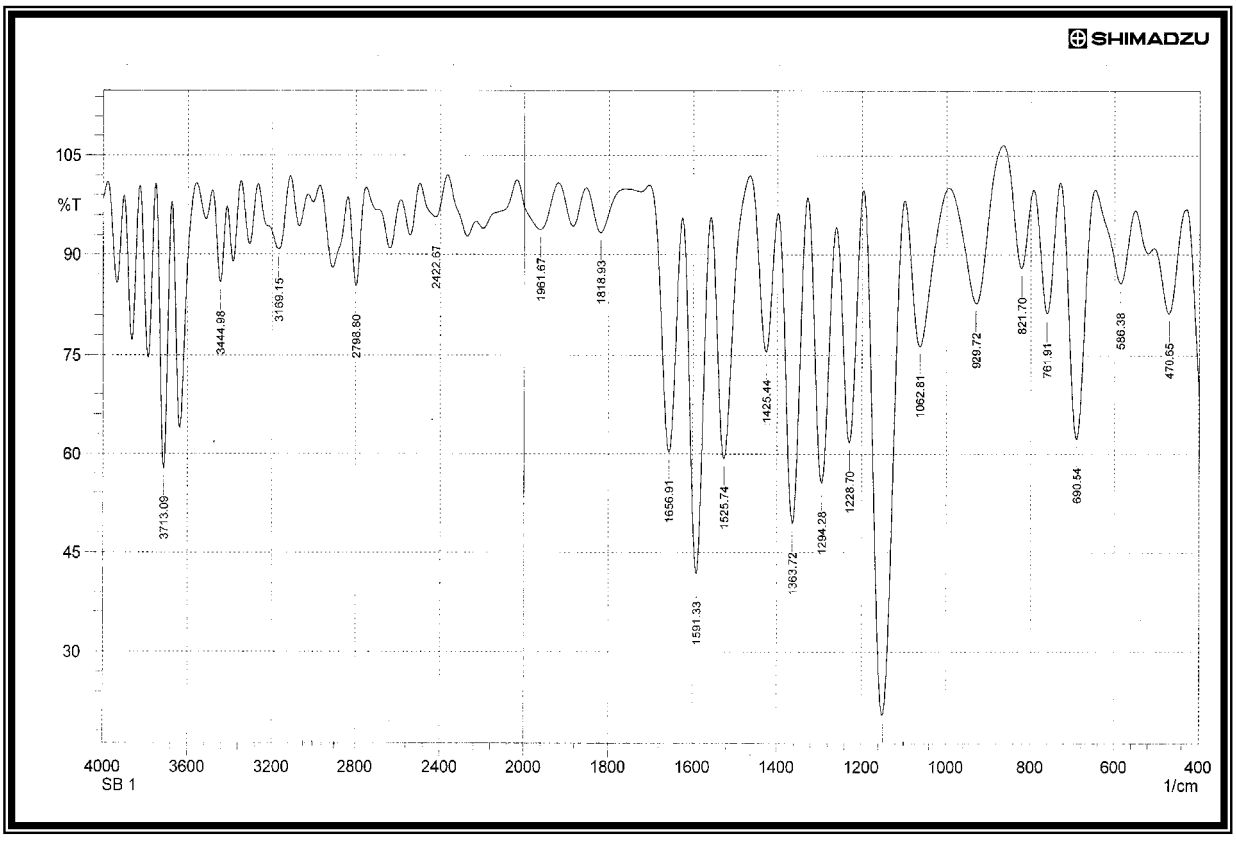
Comp No.	M.P.ºC	Yield%	M.F.	M.Wt.	Calculated			Found		
					C%	H%	N%	C%	H%	N%
[1]	108-110	---	$C_{11}H_{13}N_3O$	203	---	---	---	---	---	---
[2]	152-155	77	$C_{20}H_{22}N_4O$	334	71.85	6.58	16.76	72.03	6.67	16.88
[3]	160-162	88	$C_{21}H_{23}N_3O$	333	75.67	6.90	12.61	75.81	7.02	12.14
[4]	168-171	78	$C_{18}H_{16}BrN_3O$	370	58.37	4.32	11.35	58.44	4.21	11.19
[5]	210-212	70	$C_{24}H_{24}N_4O_4$	432	66.66	5.55	12.96	66.50	5.73	13.18
[6]	198-200	55	$C_{25}H_{25}N_3O_4$	431	69.60	5.80	9.74	70.01	5.94	9.23
[7]	190-193	60	$C_{22}H_{18}BrN_3O_4$	468	56.41	3.84	8.97	56.50	3.98	8.89
[8]	210-213	67	$C_{28}H_{26}N_4O_4$	482	69.70	5.39	11.61	69.25	5.63	11.77
[9]	206-209	59	$C_{29}H_{27}N_3O_4$	481	72.34	5.61	8.73	72.59	5.90	8.32
[10]	220-222	62	$C_{26}H_{20}BrN_3O_4$	518	60.23	3.86	8.10	60.38	3.27	8.28

Table (II): The major FT-IR absorption (cm^{-1}) of compounds [1-10]

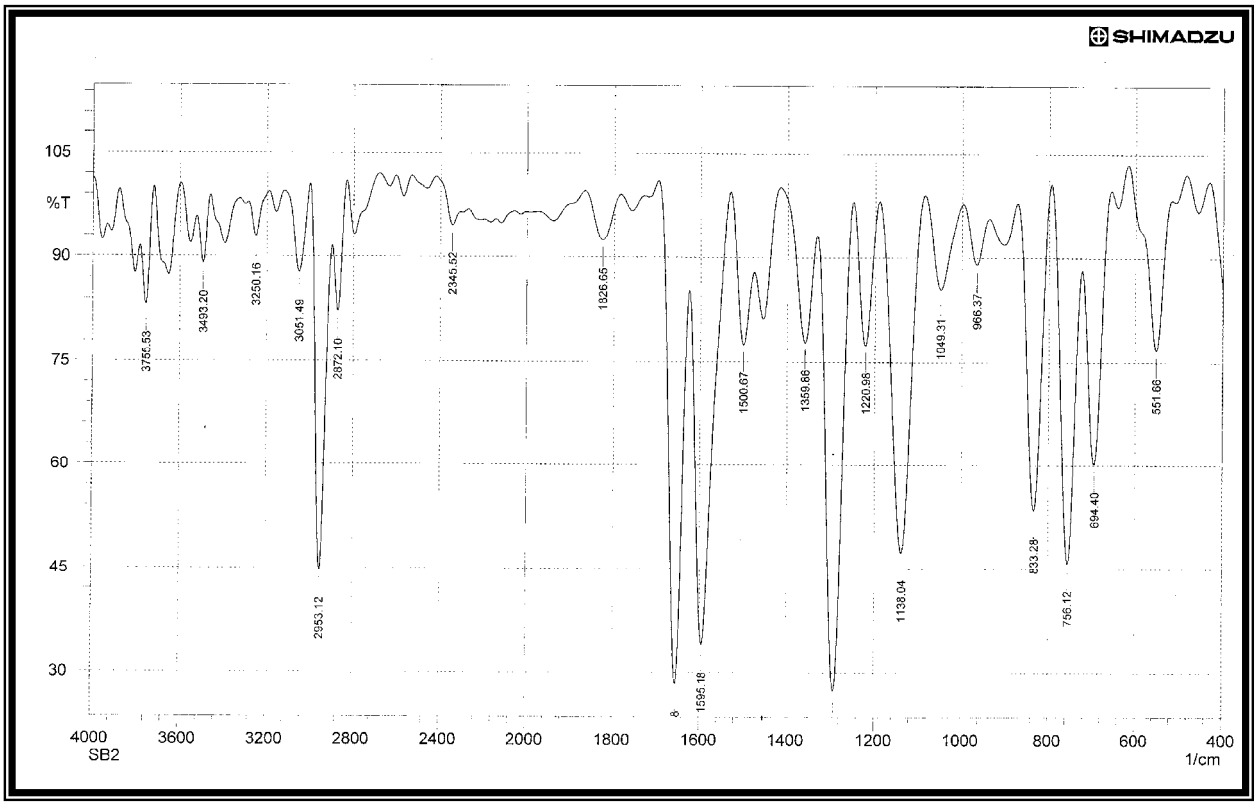
Comp No.	υ / NH_2	υ / C-H arom.	υ / C-H aliph.	υ / C=O Ketone	υ / C=O Lactone	υ / C=O Lactame	υ / C=N	υ / C=C arom.	δ / C-H arom. o.o.p.	υ / C-Br
[1]	3432 3320	3066	2895	1876	---	---	---	1579 1498 1435	839 754	---
[2]	---	3050	2900	1818	---	---	1656	1591 1525 1425	821 761	---
[3]	---	3051	2953 2872	1826	---	---	1652	1595 1500 1452	833 756	---
[4]	---	3059	2935	1818	---	---	1650	1579 1487 1419	827 761 704	509
[5]	---	3066	2926	1801	1722	1654	---	1593 1541 1489	866 825 765	---
[6]	---	3057	2958 2866	1801	1720	1653	---	1597 1558 1491	839 758	---
[7]	---	3059	2941	1803	1726	1639	---	1579 1490 1400	831 777	505
[8]	---	3093	2897	1791	1728	1664	---	1593 1535 1480	880 817 702	---
[9]	---	3061	2955 2868	1790	1730	1676	---	1595 1496 1440	880 835 758	---
[10]	---	3070	2945	1786	1722	1672	---	1637 1580 1490	829 761 705	509



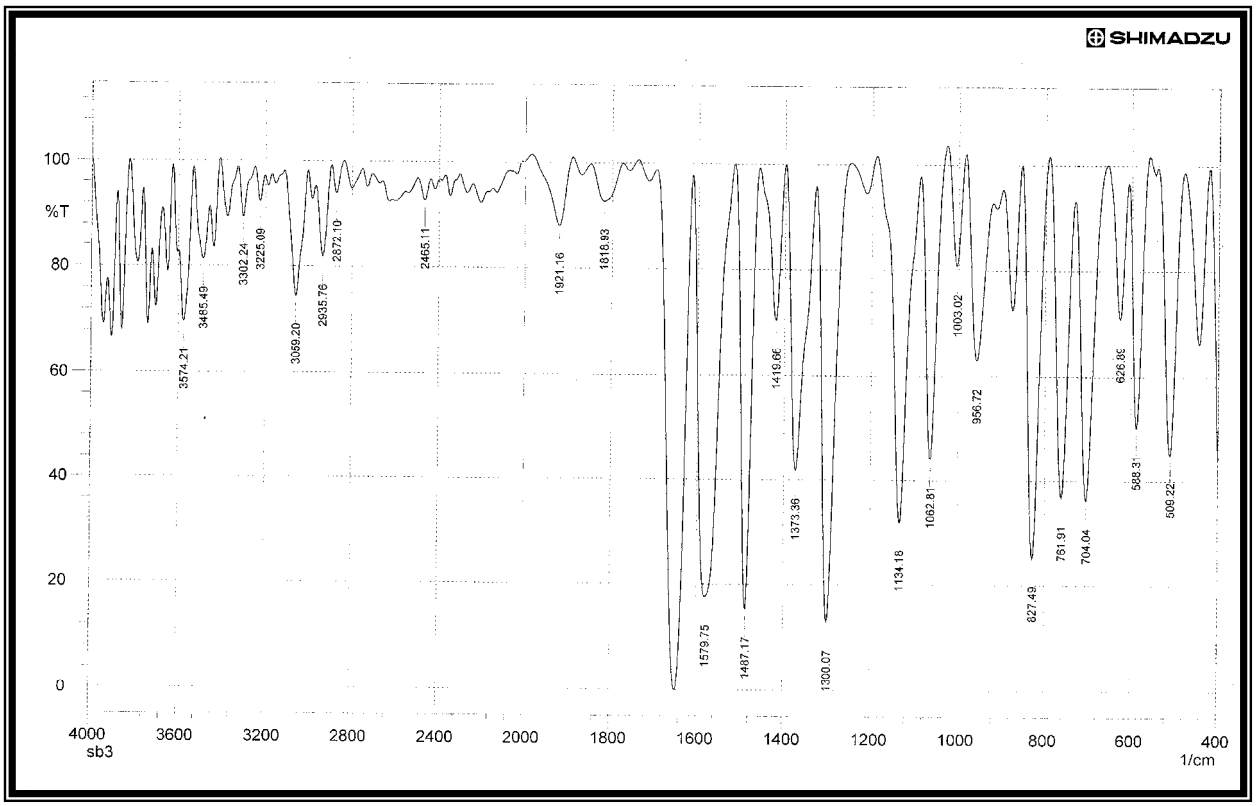
FT-IR spectrum of compound [1]



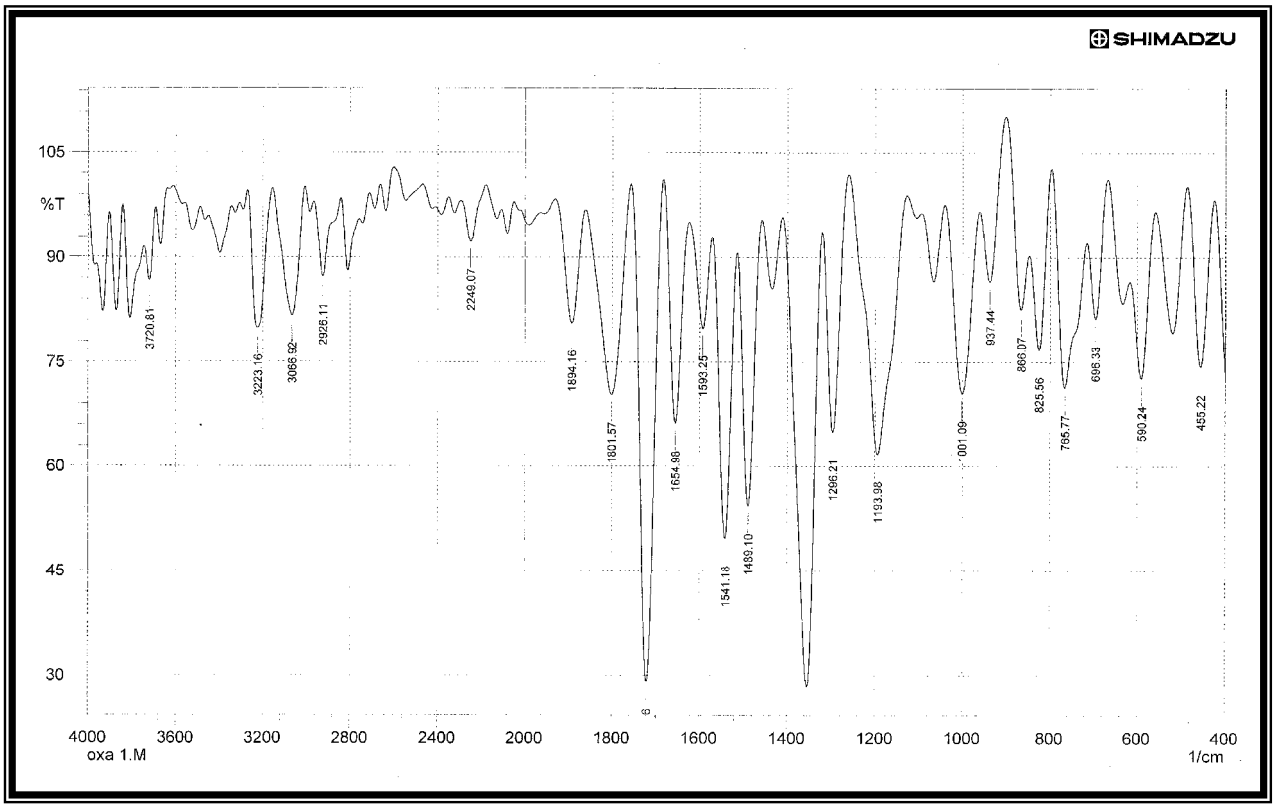
FT-IR spectrum of compound [2]



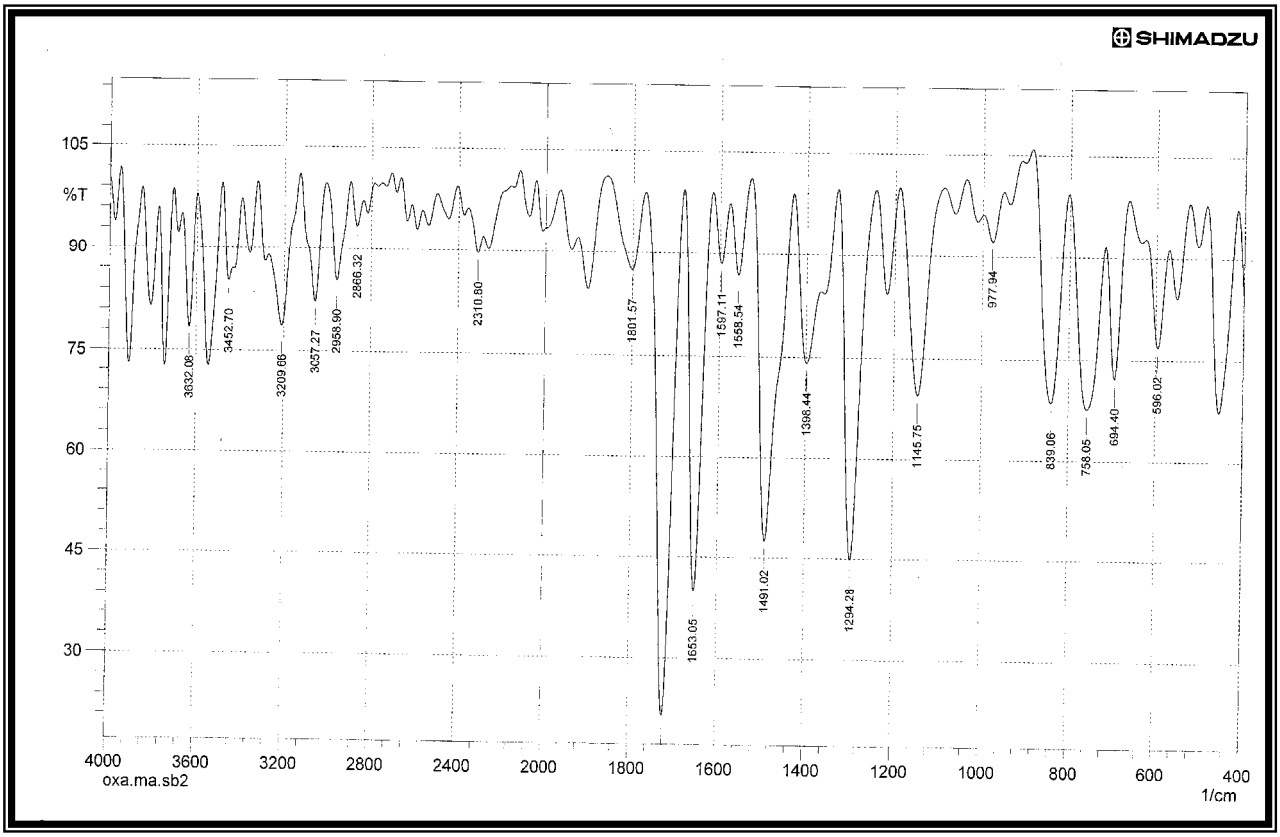
FT-IR spectrum of compound [3]



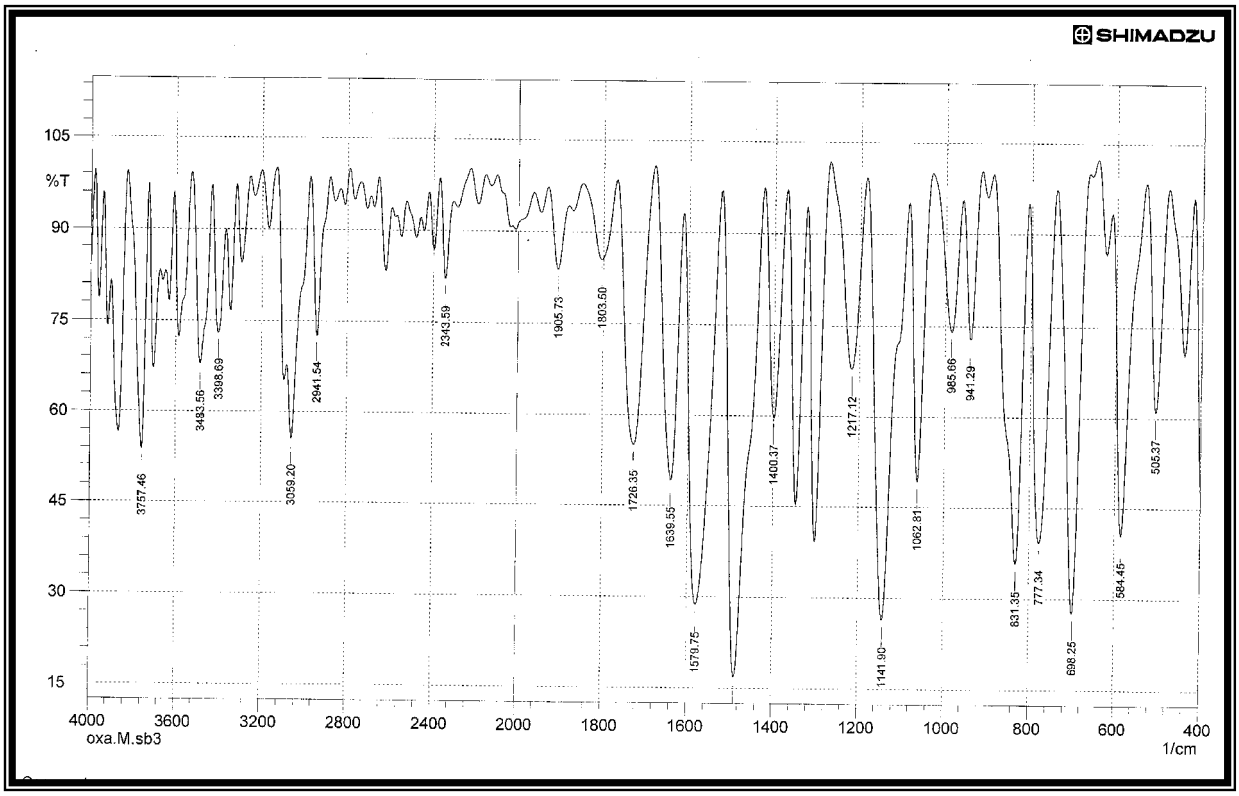
FT-IR spectrum of compound [4]



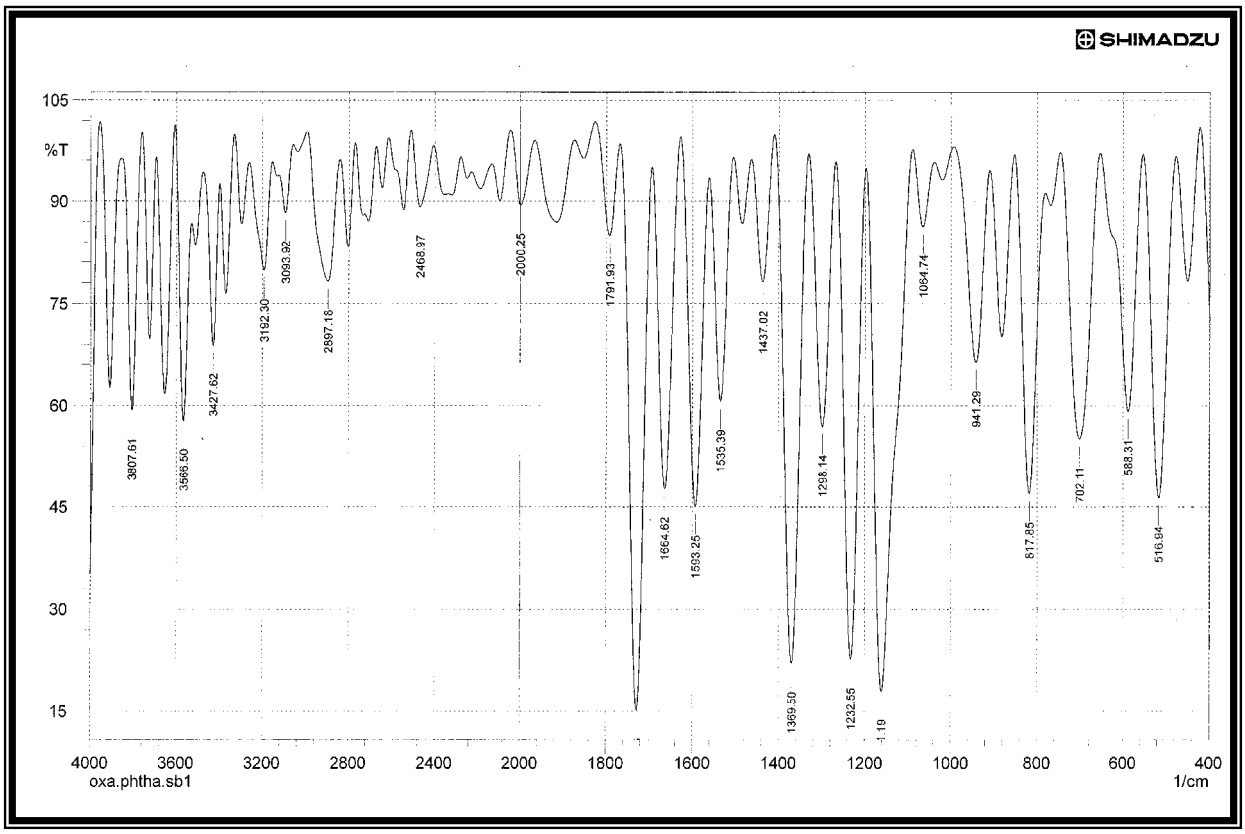
FT-IR spectrum of compound [5]



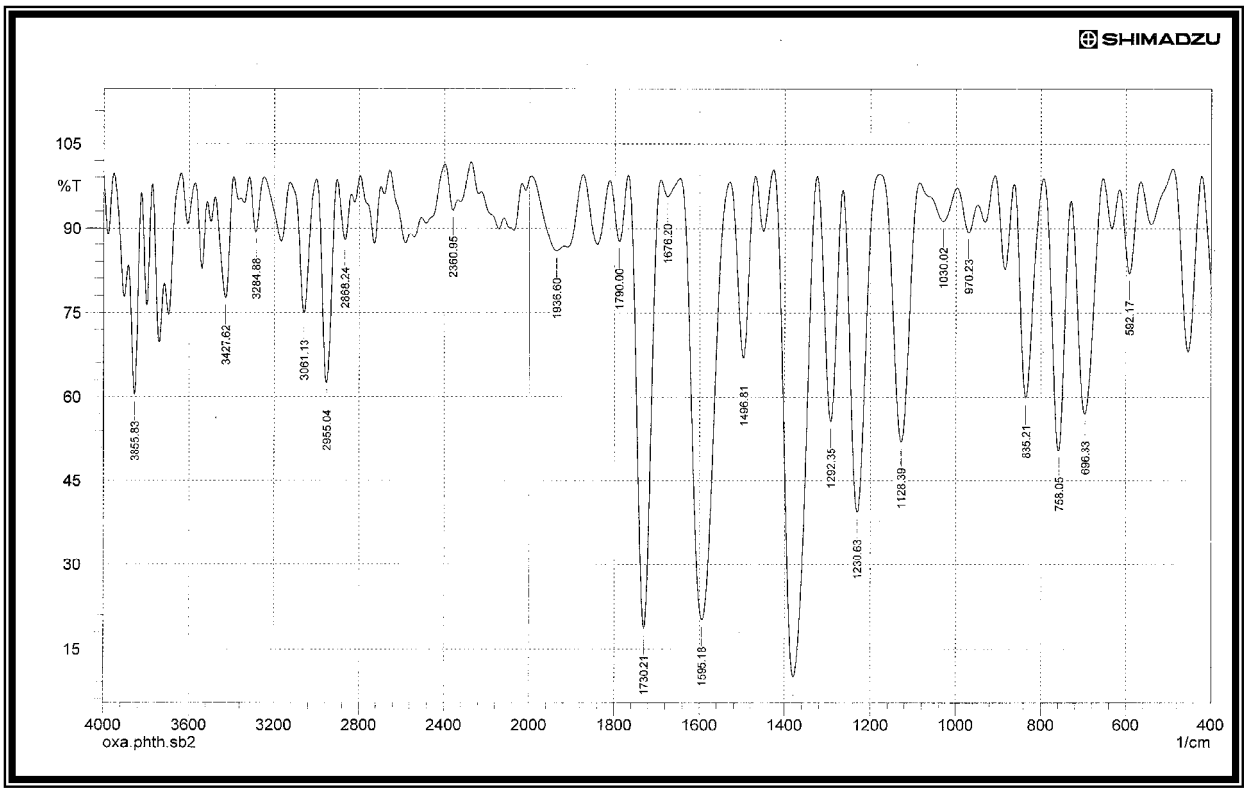
FT-IR spectrum of compound [6]



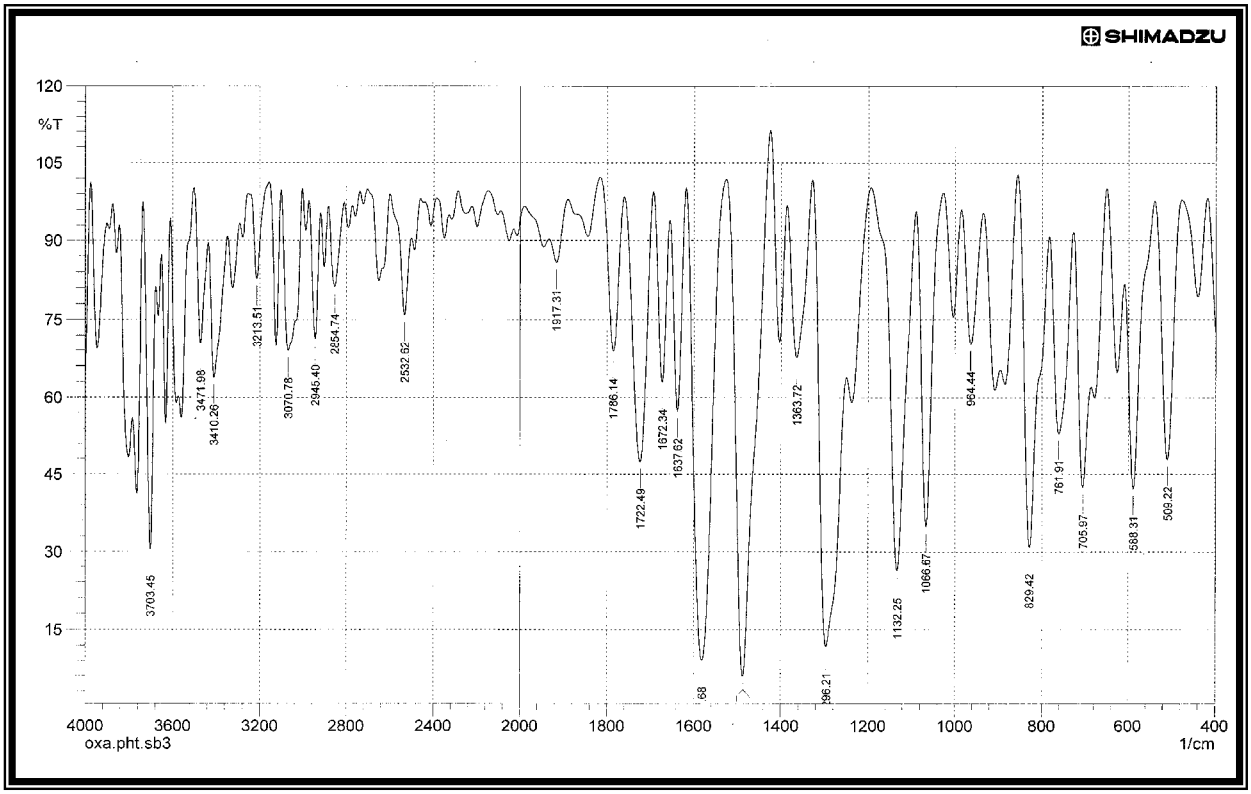
FT-IR spectrum of compound [7]



FT-IR spectrum of compound [8]



FT-IR spectrum of compound [9]



FT-IR spectrum of compound [10]

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