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Synthesis Of New Oxazole -4-One Derivatives From Phenyl Alanine

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Abstract

The present research includes the synthesis of fifteen new derivatives for the compound (1,3-oxazol-5-(4H)-one (1)) which perfect the synthesis for reaction Phenyl alanine with acetic anhydride to afford 1,3-oxazol-5-(4H)-one, which complete conversion to 3-Amino-5-benzyl-2-methyl-3,5-dihydro-4H-imidazol-4-one (2) to react with the hydrazine hydrate %99 ethanol boiling ,take on the component (2) for primary material was used because it contains the material of NH_2 active in the synthesis of several Schiffs bases (3 - 6),in order to heat them with different aromatic aldehydes or keton in the solvent ethanol. Later on several of Schiffs Bases to were used prepare a new derivatives(7 - 10) by added (benzoyl chloride) to (isomethine) (-CH=N-) group at the last compounds (11 - 14) by substituting (Cl) group in the (7 - 10) compound to group (S-C=NH NH_2) from its reaction with thiourea in the presence of (Na_2CO_3),on the other hand when the essential compound (2) is heated with bromo acetic acid in the basic midem for period of (7hours) that lead to forming the new derivatives (15) The synthesized compounds were confirmed by using some spectroscopy methods (FT-IR, UV.-Visible,C.H.N)

الخلاصه

تم في هذا البحث تحضير مركب 4-بنزايل-2-مثيل-3,1-اوكسازول-5-(4H)-اون (1) بمفاعلة الحمض الاميني (فنل الانين) مع انهدريد الخليك وبعدها حول المركب (1) الى 3-امينو-5-بنزايل-2-مثيل-5,3ثنائي هيدرو-(4H)-ايميدازول-4-اون (2) وذلك باضافة الهيدرازين المائي الى المركب (1). حضرت قواعد شيف (3-6) من اضافة الالديهايدات والكيتونات الاروماتية الى المركب (2). الاصرة المزدوجه في الايزوميثانات تم فتحها بأضافة البنزويل كلورايد للحصول على الامايدات(7-10). بعد ذلك تم ازاحة ايون الكلورايد السالب بأضافة الثايويوريا الى مشتقات الاميدازول وحسب تفاعلات الاستبدال الثنائية SN2 للحصول على مركبات الثايويوريز (11-14). الحامض الكاربوكسيلي(15) حضر باضافة كلورو حامض الخليك الى مشتق الامين. شخصت المركبات المحضرة باستخدام بعض الطرق الطيفية (FT-IR , UV,C.H.N)

Introduction

Oxazole synthesis is a chemical synthesis of the aromatic heterocyclic oxazole from cyanohydrins in the presence of anhydrous hydrochloric acid[1,2] .

Various oxidation reactions, one study reports on the oxidation of 4-5- biphenyl oxazole[3].

Imidazole has two nitrogen atoms. The one is slightly acidic while the other is basic so imidazole and its derivatives are widely used as intermediates in the synthesis of organic target compounds including pharmaceuticals, agrochemicals, dyes, photographic chemicals[4].

Schiff's bases have been shown as biologically versatile compounds having antifungal, herbicidal and plant growth[5,6].

Thioureas were synthesized by condensation of Schiff's bases with aryl chloride, then subseguenuent reaction withthiourea, which have ben shown as biologically versatile compounds having antibacterial activit[7,8]

Oxazole and Imidazole derivative have awide range of biological utilizes like anti funji,anti bacteria etc[9,10].

Many research about preparation of compounds like this work were published[11,12]

In this paper the compound of 4-benzyl-2-methyl-1,3-oxazol-5-(4H)-one and its derivatives has been synthesized

Experimental

Melting point were determined in open capillary tubes on Gallen Kamp melting point apparatus and are uncorrected. The IR spectra (KBr-discs) were recorded with a pye-Unicam Sp-300 spectrometer.

UV spectra were recorded on Hitachi-2000 spectrophotometer using absolute ethanol as solvent.

Synthesis of 4-benzyl-2-methyl-1,3-oxazol-5-(4H)-one (1)

A mixture of amino acid (2gm;0.012mol) and (10ml;0.106mol)acetic anhydride was refluxed for 40minutes.The solution was cooled to room temperature and excess acetic acid was removed by flow of nitrogen gas over the solution.

Synthesis of 3-amino-5-benzyle-2-methyl-3,5-dihydro-4H-imidazol-4-one (2)

To a solution of compound(1) (0.01mol) in(15ml) hydrazine. The mixture was refluxed for (30hrs),the solvent was removed and the solid product was collected and crystallized from Ethanol.

Synthesis of 5-benzyl-2-methyl-3,5-dihydro-4H-imidazole-4-one]-3-amino}-N acetohydrazide. (3-6)

To a stirring of compound(2) (0.01mol) in absolute ethanol (15ml),The appropriate aldehyde or ketone (0.01mol) was added, then the mixture was refluxed for (3hrs) and cooled to room temperature. The precipitate was filtered and recrystallized from appropriate solvent.

Synthesis of chloro(aryl) methyl-5-(4-benzyl)-2-methyl-3,5-dihydro4H-imidazole-4-one-3-yl)benzohydrazide. (7-10)

To a stirring solution of compound (6-10) (0.005mole) indry benzene (15ml) a mixture of (benzoylchloride) (7.08gm,0.005mole) and benzene (10ml) was added drop wise.

After that the mixture was refluxed for (1hrs) with continuous stirring, colored crystals were precipitated and recrystallized from appropriate solvent.

Synthesis of 2-methyl-5-(4-benzy)-4-oxo-imidazol-3-(4H)-yl)amino (arl)methyl imidothiocarbamate. (11-14)

In a(100ml) round bottom flask, a mixture of (0.005mole) of compounds (11-13) and (0.38gm,0.005mole) thiourea dissolved in (20ml) absolute ethanol and (0.53gm,0.005mole) of anhydrous sodium carbonate, was replaced.

The final mixture was refluxed for (4hrs) with continuous stirring.

The reaction mixture was filtered to remove sodium chloride, then the filtrate was transferred to a beaker containing ice water.

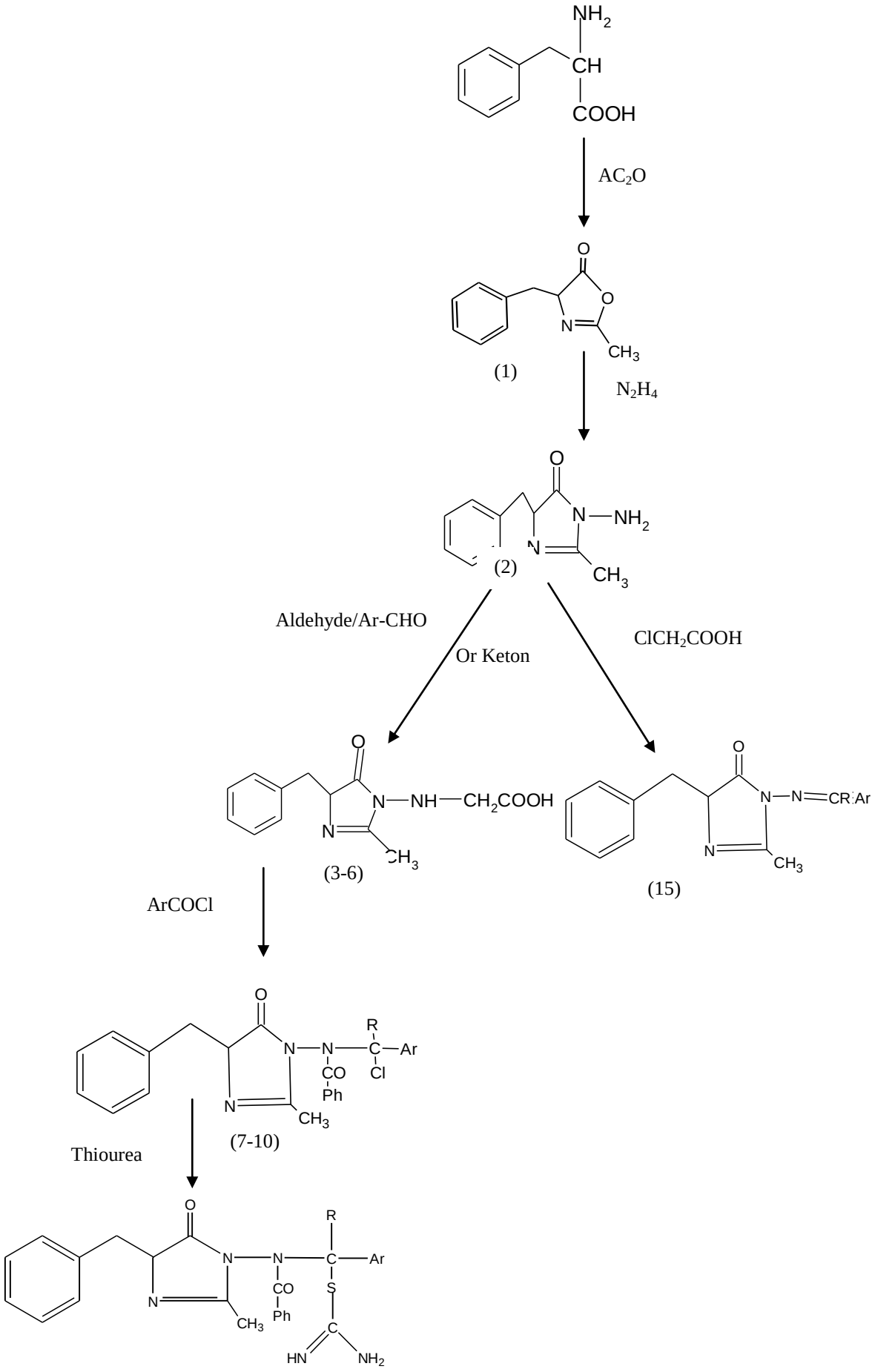
and the precipitate crystals were filtered to yield colored.

Crystals of compounds (11-14).

Synthesis of [(4-benzyl-2-methyl-5-oxo-4,5-dihdro-1H-imidazol-1-yl)amino] (15)

To a mixture of compound (2) (2gm,0.02mol) and sodium carbonate (2.21gm,0.02mol) in (20ml)water, chloroacetic acid (0.94gm,0.01ml) was added.

Then the reaction mixture was refluxed for (3hrs) after that, mixture was acidified with HCl. The precipitate was filtered and recrystalized from Ethanol.


NH2
CH
COOH
AC2O
O
O
N
CH3
(1)
N2H4
O
N—NH2
N
CH3
(2)
Aldehyde/Ar-CHO
Or Keton
ClCH2COOH
O
N—NH—CH2COOH
N
CH3
(3-6)
O
N—N=CR:Ar
N
CH3
(15)
ArCOCl
O
N—N—C—Ar
R
CO
Ph
Cl
N
CH3
(7-10)
Thiourea
O
N—N—C—Ar
R
CO
Ph
S
C
HN
NH2
N
CH3
(11-14)

Scheme (1)

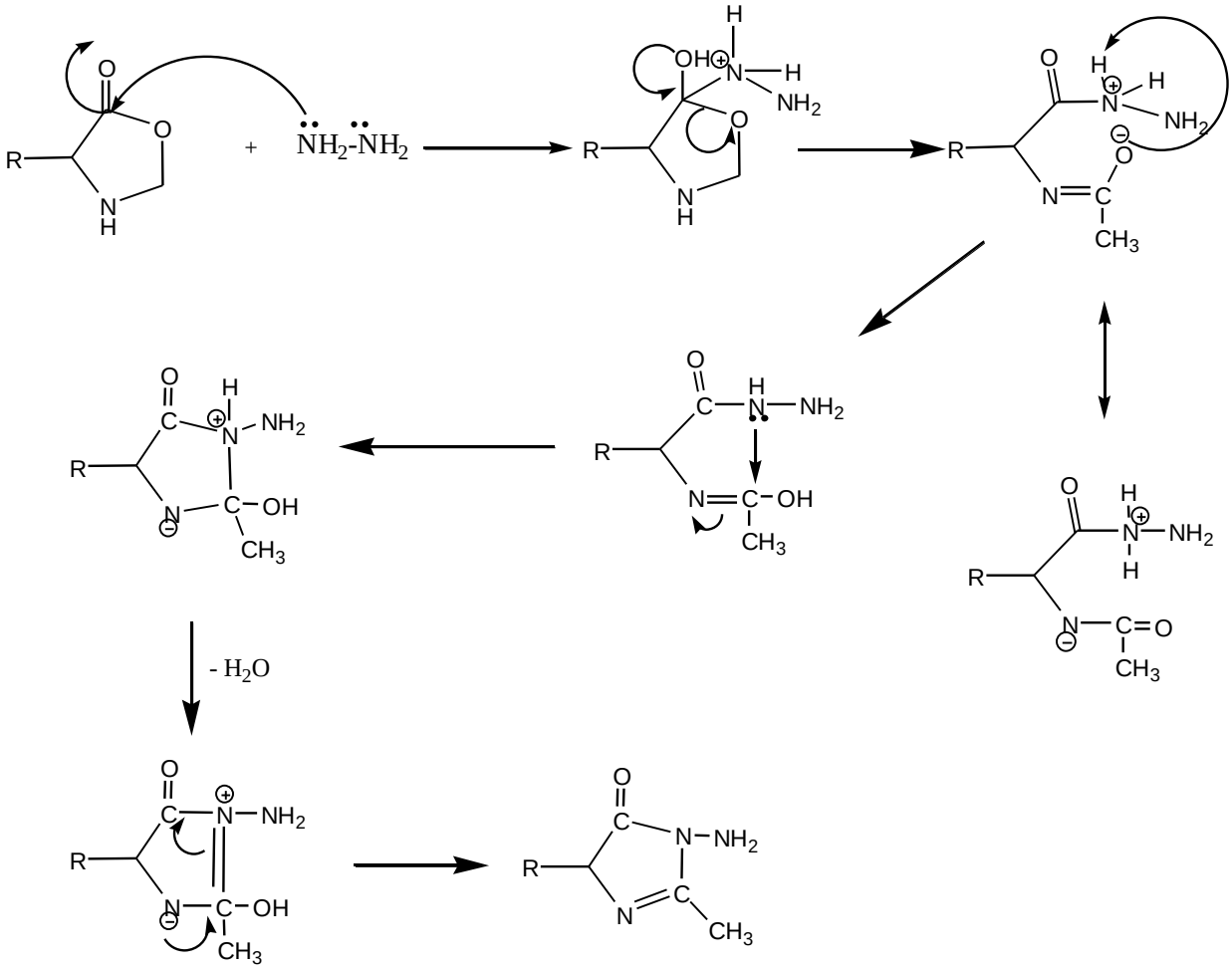
Result and Discussion

We reported the synthesis of new heterocyclic derivatives containing phenyl moiety were prepared.

Compound (1) was afforded from reaction of phenyl alanine with acetic anhydride, the reaction sequins outlined in (scheme 1).

The IR spectra of compound (1) showed the increasing in carbonyl frequency and disappearance of the OH stretching band .UV. spectrum showed max at(294nm) and(282nm) due to $\mathbf{n} \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ respectively.

Compound (2) was obtained from reaction of compound above reaction (scheme 2):



R = Ph-CH_2

Scheme 2

The IR spectrum of compound (2) showed the decreasing frequency of carbonyl group from (1666 cm -1) and appearance of the NH2 stretching bands at (3375-3210 cm -1).

The UV spectrum above compound showed two intense maxima at (305 nm) and (277 nm) Which belong to $\mathbf{n} \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ and transitions respectively

Another Schiff bases derivatives (9-6) were prepared by condensation of amino group for imidazole derivative (2) with aryl aldehydes or ketons in absolute ethanol.
Azomethine group (CH=N) appearance at1620 – 1635 cm -1. The UV. Spectra showed two intense maxima at 273-296 nm and at 297-535 nm due to $\mathbf{n} \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions respectively
.The reaction of the above Schiff bases (9-6) with benzoyl chloride and subsequent reaction of above reaction products (10-7) with thiourea were carried out.
Moreover treatment of Schiff bases with the above acid chloride results in the formation of (10-7) in which the two groups Cl and ArCO) were introduced in the same step of reaction. This reaction was followed by appearance of absorption bonds at 1591-1665 cm -1 and at 698-7 94 cm -1 due to C=O and C-Cl moieties respectively
The reaction of products (10-7) with thiourea afforded thioureas products (14-11).
These compounds (14-11) were characterized by their IR and UV . Spectra . New doublet absorption bands in the region 3351-3385 cm -1 were attributed to NH2 and at 3171-3190 due to NH. Other characteristic bands in the region 1061-1090 cm -1 correlated to C-S moiety.
Moreover the band of C-Cl has disappeared.
U.V spectra of compounds (14-11) showed intense bands at 304-360 nm and 286-300 which belong to $\mathbf{n} \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions respectively

Table -1: physical properties and CHN analyses of compounds 1-2 (purification solvent is Ethanol)

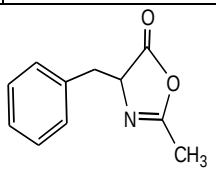
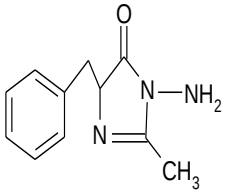
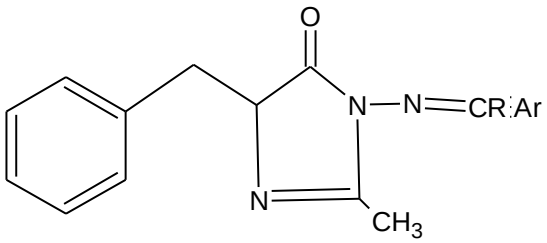
Comp .No.	Structure	Mp/°C	yield %	Formule	Found %			Theoritical %		
					C	H	N	C	H	N
1		128-130	81	$C_{11}H_{11}NO_2$	69.82	5.79	7.39	69.84	5.82	7.40
2		157-159	70	$C_{11}H_{13}N_3O$	65.1	6.38	20.67	65.02	6.40	20.68

Table -2: physical properties and CHN analyses of compounds 3-6 (purification solvent is Ethanol)



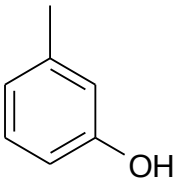
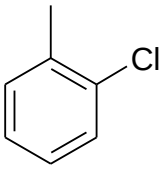
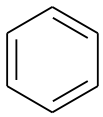
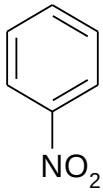
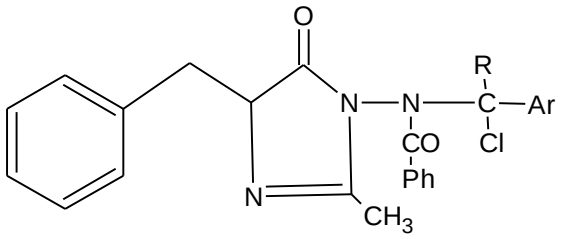
com. No.	R	Ar	Mp/° C	yield %	Formule	Found %			Theoritical %		
						C	H	N	C	H	N
3	H		oily	75	$C_{18}H_{17}N_3O_2$	70.38	5.54	13.66	70.38	5.53	13.68
4	H		oily	71	$C_{18}H_{16}N_3OCl$	66.37	4.92	12.88	66.35	4.91	12.90
5	Ph		oily	63	$C_{24}H_{21}N_3O$	58.93	5.72	11.46	58.95	5.71	11.44
6	Ph		139-141	60	$C_{24}H_{20}N_4O_3$	69.88	4.83	13.61	69.90	4.85	13.59

Table -3: physical properties and CHN analyses of compounds 7-10(purification solvent is Benzene)



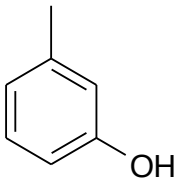
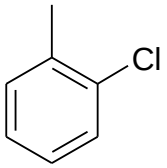
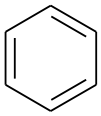
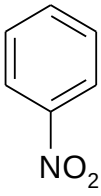
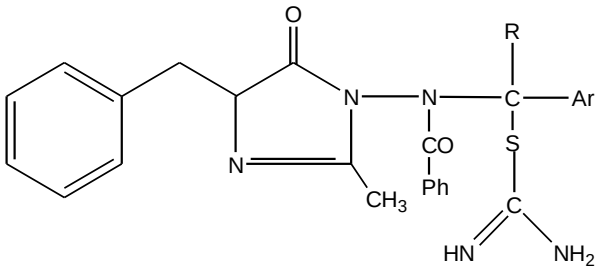
Comp. No.	R	Ar	Mp/°C	yield %	Formule	Found %			Theoritical %		
						C	H	N	C	H	N
7	H		280 (dec.)	52	$C_{25}H_{22}N_3O_3Cl$	67.08	4.93	9.4	67.03	4.91	9.38
8	H		300 (dec.)	55	$C_{25}H_{21}N_3O_2Cl_2$	64.39	4.51	9.2	64.37	4.50	9.01
9	Ph		oily	41	$C_{31}H_{26}N_3O_2Cl$	73.50	5.14	8.30	73.30	5.12	8.27
10	Ph		oily	43	$C_{31}H_{25}N_3O_4Cl$	69.11	4.65	7.77	69.08	4.64	7.79

Table -4: physical properties and CHN analyses of compounds 11-14 (purification solvent is Ethanol and Ethanol:H_2O)



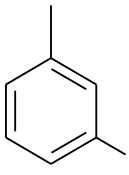
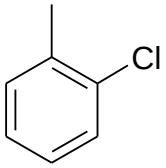
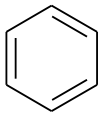
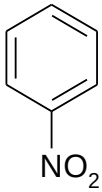
Comp. No.	R	Ar	Mp/°C	yield %	Formule	Found %			Theoritical %		
						C	H	N	C	H	N
11	H		205-207	65	$C_{26}H_{26}N_5O_3S$	64.10	5.38	14.39	64.06	5.33	14.37
12	H		187-188	50	$C_{26}H_{25}N_5O_2SCl$	61.70	4.92	13.82	61.72	4.93	13.84
13	Ph		178-181	40	$C_{32}H_{30}N_5O_2S$	70.24	5.53	12.81	70.20	5.48	12.79
14	Ph		oily	42	$C_{32}H_{29}N_5O_4S$	66.44	5.11	12.09	66.43	5.01	12.11

Table -5: physical properties and CHN analyses of compound 15(purification solvent is Ethanol)

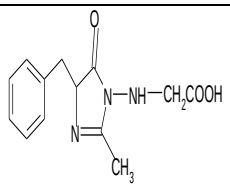
Comp. No.	Structure	Mp/°C	Yield %	Formule	Found %			Theoritical %		
					C	H	N	C	H	N
15		oily	61	$C_{13}H_{15}N_3O_3$	59.78	5.77	16.10	59.77	5.74	16.09

Table -6: spectra data of compounds (1-2)

Comp No.	UV. (EtOH) λ_{max}	Characteristic band of IR spectra (cm^{-1}) KBr disc						
		$\upsilon(C-H)_{al}$	$\upsilon(C-H)_{ar}$	$\upsilon(NH)$	$\upsilon(NH_2)$	$\upsilon(C=O)$	$\upsilon(C=C)$	other
1	294 282	2928 2874	3026	- - -	- - - -	1718	1618 1500	υ(C-O) 1209 υ(C=N)1541
2	305 277	2970 2880	3060	- - -	3375 3210	1666	1580 1439	υ(C-N)1300 υ(C=N)1577

Table -7: spectra data of compounds (3-6)

Comp No.	UV. (EtOH) λ_{max}	Characteristic band of IR spectra (cm^{-1}) KBr disc					
		$\upsilon(C-H)_{al}$	$\upsilon(C-H)_{ar}$	$\upsilon(C=O)$	$\upsilon(C=N)$	$(C=C)_{ar}$ υ	other
3	511 289	2960 2885	3080	1635	1620	1585 1519	3414 υ(OH)
4	301 275	2945 2850	3093	1639	1635	1579 1516	750 υ(C-Cl)
5	536 296	2956 2860	3085	1649	1625	1578 1514	
6	297 273	2935 2810	3090	1651	1630	1589 1516	1454-1369 $\upsilon(N0_2)$

Table -8: spectra data of compounds (7-10)

Comp No.	UV. (EtOH) λ_{max}	Characteristic band of IR spectra (cm^{-1}) KBr disc					
		$\upsilon(C-H)_{al}$	$\upsilon(C-H)_{ar}$	$\upsilon(C=O)$ Lactam	$\upsilon(C=O)$ amide	$\upsilon(C=C)_{ar}$	other
7	558 300	2973 2856	3066	1651	1630	1589 1500	3414 υ(OH) 700 υ(C-Cl)
8	360 297	2875 2843	3032	1703	1665	1600 1502	794 υ(C-Cl)
9	551 297	2887 2839	3055	1700	1627	1595 1480	698 υ(C-Cl)
10	519 299	2967 2851	3097	1657	1591	1570 1485	1491-1387 $\upsilon(NO_2)$ 702 υ(C-Cl)

Table -9: spectra data of compounds (11-14)

Comp No.	UV. (EtOH) λ_{max}	Characteristic band of IR spectra (cm^{-1}) KBr disc						
		$\upsilon(C\text{-}H)_l$	$\upsilon(C\text{-}H)_{ar}$	$\upsilon(C=O)$ Lactam	$\upsilon(C=O)$ amide	$\upsilon(NH)$	$\upsilon(NH_2)$	other
11	304 286	2985 2863	3097	1710	1650	3178	3381 3279	1076 υ(C-S) 3411 υ(OH)
12	325 292	2889 2837	3066	1700	1635	3190	3352 3215	1063 υ(C-S) 794 υ(C-Cl)
13	360 297	2875 2810	3097	1703	1626	3171	3379 3279	1091 υ(C-S)
14	345 300	2978 2812	3035	1692	1676	3184	3377 3288	1016 υ(C-S) 1541-1404 $\upsilon(NO_2)$

Table -10: spectra data of compounds (15)

Comp No.	UV. (EtOH) λ_{max}	Characteristic band of IR spectra (cm^{-1}) KBr disc				
		$\upsilon(C\text{-}H)_{al}$	$\upsilon(C\text{-}H)_{ar}$	$\upsilon(NH)$	$\upsilon(C=O)$ Lactam	other
15	335 285	2920 2810	3034	3356	1622	1722 υ(C=O)acid

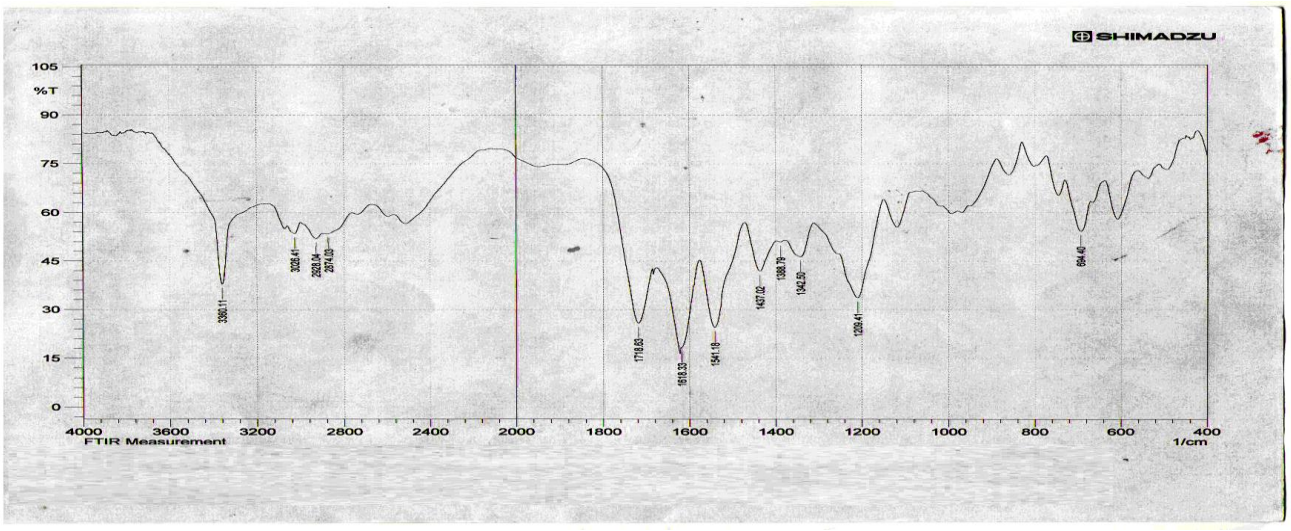


Figure (1) FTIR spectrum of compound (1)

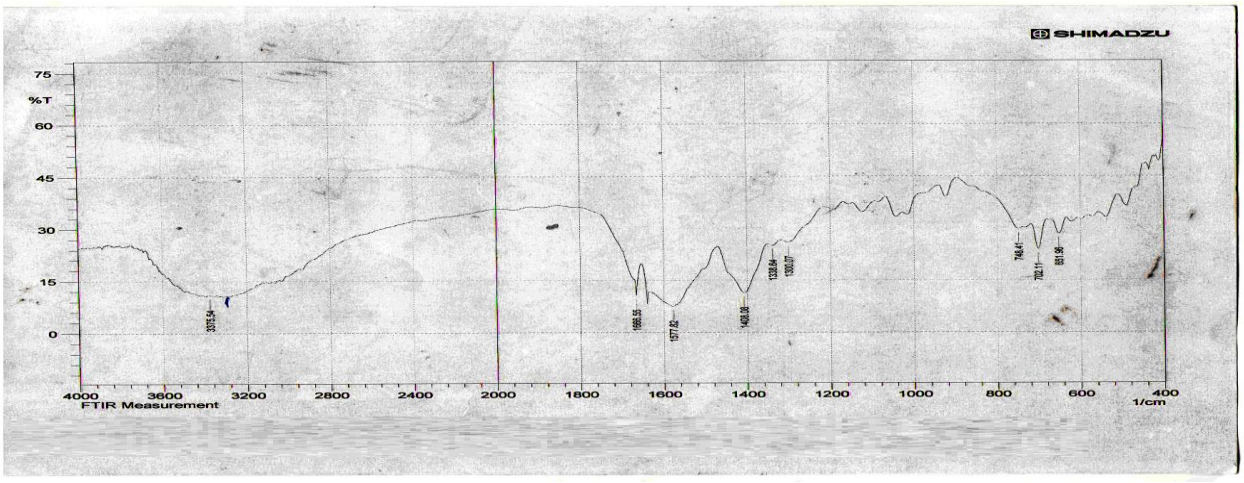


Figure (2) FTIR spectrum of compound (2)

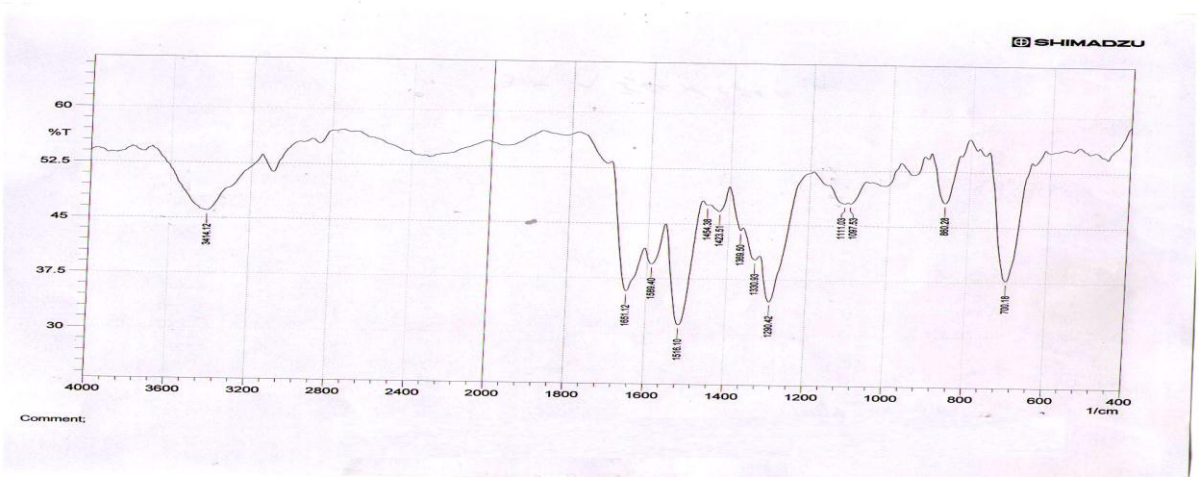


Figure (3) FTIR spectrum of compound (6)

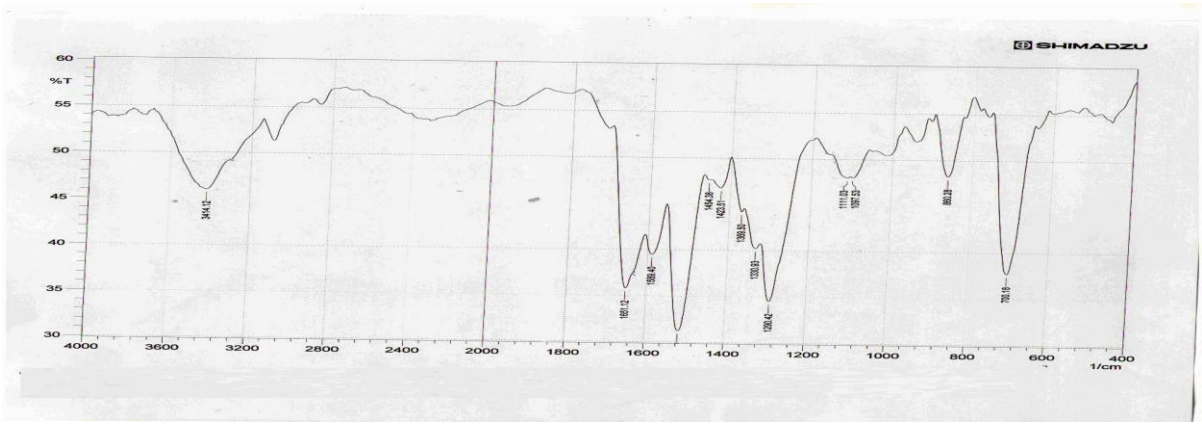


Figure (4) FTIR spectrum of compound (7)

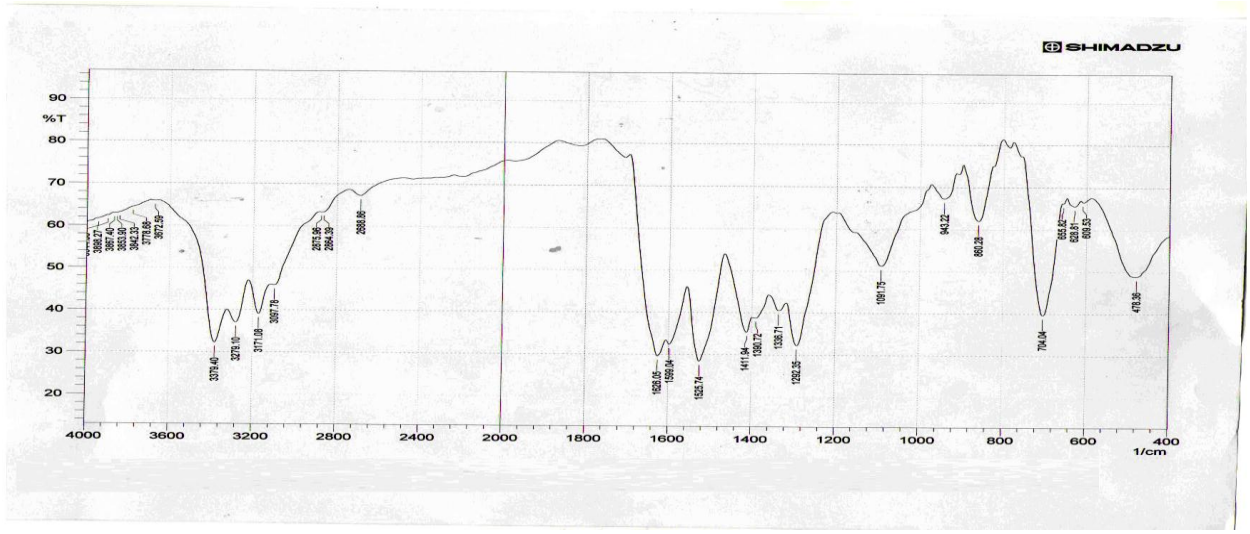


Figure (5) FTIR spectrum of compound (13)

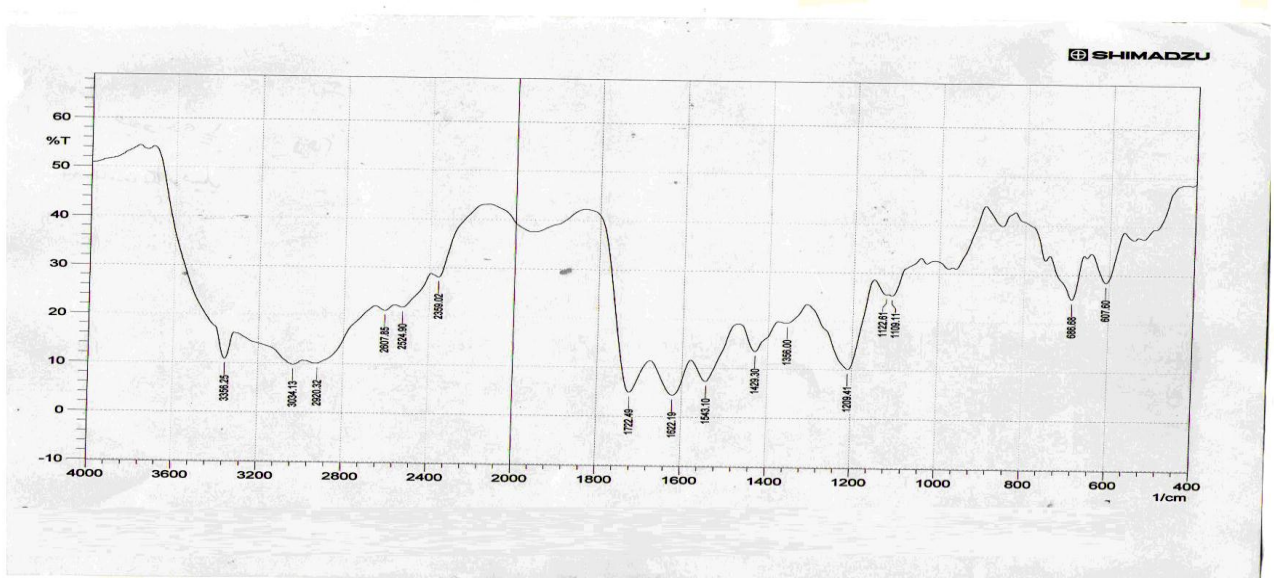


Figure (6) FTIR spectrum of compound (15)

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