Synthesis and Identification some of heterocyclic compounds from imidazole derivatives

Shaimaa Adnan College of Education, University of Al-Qadisiya shemaadnan@yahoo.com

Kasim Hassan

College of Science, University of Babylon Hassan Thamer

College of Education for Women-University of Kufa

(NJC)

(Received on 10/6/2013) (Accepted for publication 15/8/2013)

Abstract

This reserch involved hetrocyclic compounds such as (β-Lactam derivatives, Thiazolidine-4- one derivatives, midazolidin-4-one derivatives) were prepared by reaction between 4 -(1H-benzo [d]imidazol -2-yl aniline (1) with p-amino acetophenone to get N-(1- (4-aminophenyl) ethylidene) -4-(1H - benzo[d] imidazol -2-yl)aniline(2) which reacts with substutid aromatic aldehyde to get 4-(1-((4-(1H-benzo [d] imidazol -2- yl) phenyl) imino)ethy l) -N-(derivative benzylidene) aniline. The cyclization of (3-6) with chloroacetylchloride, thioglycollicacid and α-aminoacid such as glycine and aniline give the corresponding β-lactam (7-10), thiazolidine-4-one (11-14) and imidazolidine-4-one (15-22) derivatives.

.All this compounds characterized by means of FT- IR, ¹H-NMR, and follow reaction by R_f- TLC and Measure melting point .

Key words:- heterocyclic, benzoimidazole, β-Lactam, Thiazolidin, Imidazolidin

الخلاصة

تضمن البحث تحضير مركبات حلقيه غير متجانسة مثل (مشتقات البيتا لاكتام , مشتقات الثايوزولدين-4- اون , مشتقات الاميدازولدين -4 اون) التي تم تحضيرها من تفاعل 4 (1-هيدروجين بنزو (د) اميدازل 2-ايل) انلين(1) مع بارا -امينو اسيتوفينون لنحصل على نتروجين - (1 - (4 -امينوفنيل) اثيل دايين- - (- هيدروجين -1 بنزو (د) -1 معوضة لنحصل على -1 الذي يتفاعل مع الديهايدات اروماتيه معوضة لنحصل على -1(-4 - -1 التحلق مع كلورو استايل كلورايد و حامض الثايوكلايكول والاحماض الامينيه (الكلايسين و الانين) يعطى بالمقابل البيتا لاكتام (7−10) والثايوزولدين −4− اون (11−14) والاميدازولدين (15−22) كمشتقات . كل هذه المركبات تم تشخيصها بوساطة مطيافيه الاشعه تحت الحمراء وبعضها بوساطة مطيافية الرنين النووي المغناطيسي و متابعة التفاعل بكروموتوغرافيا الطبقة الرقيقه وقياس درجة الانصهار.

الكلمات المفتاحية : - المركبات الحلقيه غير المتجانسة,البنزو اميدازول,بيتا لاكتام, ثايوزولدين , اميدازولدين

Introduction

Benzimidazole derivatives play important role in medical field with many pharmaco-

logical activities such as antimicrobial, antiviral, antidiabetic and anticancer activity. It is an important pharmacophore in drug discovery due to being a good bioisostere of naturally occurring nucleotides (1-4)

All β -lactam compounds contain a fourmember ring. While β -lactam compounds were discovered in filamentous fungi, actinomycetes and gram-negative bacteria are also known to produce different types of β -lactams (5-7)

Imidazolidin-4-ones represent an interesting class of compounds with respect to biological activity. Through manipulation of the substituents around the imidazolidin-4-one core, molecules with a variety of biological properties have been discovered. Examples include compounds that exhibit antibacterial activity. Imidazolidin - 4- one have also been reported to inhibit binding of

vascular cell adhesion molecule 1 (VCAM 1) to very late antigen 4 (VLA - 4), which are useful in treating inflammation associated with chronic inflammatory diseases such as rheumatoid arthritis, multiple sclerosis, asthma, and inflammatory bowel disease (8,9)

The versatile uses of thiazolidinones as anaesthetics 1 , anti-convulsants 2 , amoebicides 3 ,

hypotensive4 and tuberculostatic agents5 have stimulated a considerable interest to explore the possible synthesis of new potential compounds in which the thiazolidinone ring is fused with another biologically active nucleus. With a view

in achieving such a system, thiazolidine was fused with benzimidazole. (10-16)

Experimental Apparatus

(FTIR)Spectra(4000-400cm-1)in KBr disk were recorded on aSHIMADZU FTIR-8400S fourier.transform. melting point were measured using Stuart, UK. ¹HNMR were recorded on fourier transformation bruker spectrometer ,operating at (400MHz) with (DMSO-ds) measurments were made at Department of chemistry ,kashan university .Iran.

Synthesis of 4-(1H-benzo[d]imidazol-2-yl)aniline (1)

Equimolar quantities (0.01mol) of *o*-benzen diamine, *p*-amino benzoic acid (0.01 1mol) in 4N HCl (20mL)was refluxed for 30 min. The mixture is cooled and filtered off. The residue is the 4-(1*H*-benzo[*d*] imidazol-2-yl)benzenamine The product is recrystallized from absolute alcohol. (17) synthesis N-(4-aminophenyl)

ethylidene)-4- (1H-benzo[d] imidazol-2-yl) aniline (2)

A mixture of equimolar quantities (0.01mol) of p-aminoacetophenone and 4-(1H- benzo [d] imidazol-2-yl) benzenamine was refluxed for 2h in 20 mL of ethanol. The reaction mixture was cooled and kept for 24 hs. The crystals found was filtered , dried and recrystallized from ethanol to give compound (2) .

General method of synthesis of compounds have tow group schiff bases (3-6)

A mixture of equimolar quantities (0.01mol) of aromatic benzaldehyde and compound(2) was refluxed for 20 min in 30 mL of ethanol. The reaction mixture was cooled and kept for (24 hs). The

crystals found was filtered, dried and recrystallized from ethanol to give compounds (3-6).

General method of synthesis of azetidinones (7-10)

A mixture of schiff bases(3-6) (0.001mol) and triethylamine (0.006mol) was dissolved in 1,4 – Dioxan (25mL), to this well stirred cooled solution of chloro acetyl chloride (0.0024mol)was added drop wise at10°C. The reaction mixture was stirred for 6 hs. Half of the solvent separated and yield 1-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-3-chloro-4-(4-(3-chloro-2-(derivatives) phenyl) -4-oxoazetidin-1-yl)phenyl) -4-methylazetidin -2- one recrystallized from chloroform.

General method of synthesis of thiazolidinones (11-14)

A mixture of schiff bases (3-6)(0.001 mol) and thioglycollic acid (0.002mol)dissolved in 1.4 dioxane(20mL), anhydrous zinc chloride(0.7mg)was added and refluxed for 8 h. The reaction was then cooled and the resulting solid was washed with sodium bicarbonate solution and final compound 3- (4-(1H-benzo[d] imidazol-2 -yl) phenyl) -2- (4 (2- (substituted)

phenyl) - 4 -oxothiazolidin-3-yl) phenyl) - 2 — methylthiazolidin -4- one recrystallized from absolute ethanol.

General method of synthesis of imidazolidin-4-one derivative (15-18)

A mixture of schiff bases(3-6) (0.001mol) dissolved in THF (15mL) and glycine (0.002mol)was dissolved in THF (15mL)and refluxed for 24 hs. The reaction was then cooled and the resulting final compound 3-(4-(1H-benzo [d] imidazol-2-yl)phenyl)-2-(4-(2-(substituted)phenyl) -5-oxoimidazolidin-1-yl) phenyl) -2-methylimidazolidin-4-one recrystallized from absolute ethanol.

General method of synthesis of 5-methyl imidazolidin-4-one derivative (18-22)⁽¹⁷⁾

A mixture of schiff bases (3-6) (0.001mol) and alanine (0.002mol)) was dissolved in THF (15mL) and refluxed for 24 hs. The reaction was then cooled and the resulting final compound 3-(4-(1H-benzo [d] imidazol -2-yl) phenyl) -2-(4-(2- (substituted) phenyl) -4-methyl -5-oxoimidazolidin -1-yl) phenyl) -2,5-dimethyl imidazolidin -4 - one recrystallized from absolute ethanol.

R:-P-N(CH3)2 ; P-Cl ; p-OH,m-OCH3 ; H5,9,13,21 3,7,11,19 4,8,12,20 6,10,14,22

Schem1

Results and Discussion

4-(1H-benzo[d]imidazol-2-yl)aniline (1)

The compound(1) was obtained as paly yellow solid yield 76.98%, M.P(209-211)°C

The infrared spectrum data of compound (1) showed band at (3047) cm⁻¹ for (Ar-H), (3394-3448) cm⁻¹ (N-H), (1319) cm⁻¹ (C-N),(1704) cm⁻¹ (C=N).

Schiff base N-(1-(4-aminophenyl)ethylidene)-4-(1H-benzo[d]imidazol-2-yl) aniline (2)

This compound was obtained as purple solid yield 94.1%, R_f =064, M.P (220) O C. The infrared spectrum data of compound (2) show absorption at (3047) cm $^{-1}$ for (Ar-H),(3332-3394) cm $^{-1}$ (N-H), (1319)cm $^{-1}$ (C-N),(1612) cm $^{-1}$ (C=N),and show new band at (2993) for (C-H)CH₃⁽¹⁷⁾

The¹H-NMR(CDCl₃) spectrum data of compound (2) show δ :6.8-7.79(m,12H,Ar-H), 4.5(s,2H,NH,NH₂), 2.8(m,6H,CH₃).

Synthesis compound (3-6) have two group of schiff base by react between (2) and sub-aromatic aldehyde.

compound (3) 4-(((4-(1-((4-(1H-benzo[d]imidazol-2-yl)phenyl) imino) ethyl) phenyl) imino)methyl)-N,N-dimethylaniline was obtained as orang

solid yield 92.28%, Rf =0.62, M.P(240) $^{\circ}$ C.

compound (4) 4-(1-((4-(1H-

benzo[d]imidazol-2-

yl)phenyl)imino)ethyl)-N-(4-chloro benzylidene)aniline was obtained as brown solid yield 20.79%,Rf =0.375,M.P (140d.)^OC.

compound (5) 4-(((4-(1-((4-(1H-benzo[d]imidazol-2-yl)phenyl)imino) ethyl) phenyl) imino) methyl)-2-methoxyphenol was obtained as orang solid yield 46.1%, Rf =0.2, M.P(163d.)°C.

The H-NMR(CDCl₃) spectrum data of compound (5) show δ :7-8(m,15H,Ar-H), 9.5 (s,1H,NH), 3.6(m,3H,OCH3), 2.1(S,3H,CH3), 8.4(s,1H,CH).

compound (6) 4-(1-((4-(1H-benzo[d]imidazol-2-yl) phenyl) imino) ethyl) -N-benzylidene aniline was obtained as goldenrod solid yield 46.1%, Rf=0.2, M.P (163d.) $^{\rm O}$ C.

The infrared spectrum data of compound (3-6) show absorption at (3047-3209) cm⁻¹ for (Ar-H),(3317-3363) cm⁻¹ (N-H), (1426-1450)cm⁻¹ (C-N),(1650)cm⁻¹ (C=N),and show band at (2839-2962) for (C-H)CH₃,compound(4)showband at(771) cm⁻¹ for (C-Cl) , compound(5)showband at(1218) cm⁻¹ for (C-O) C-OH ,(1026) cm⁻¹ (C-O) Ph-O-CH₃fig(3 ,4,5,6)⁽¹⁸⁾

Table (1) initiated spectium data for initidazondii-4-one delivatives compounds (1,2,5,4,5,0)									
Comp.	υAr-H	υN-H	υC-N	υC=N	υC-H	υC=O	υC-Cl	υOH	υArOCH ₃
	arom.				aleph.				CO
1	3047	3394	1319	1704					
2	3047	3394	1427	1704	2993				
3	3055	3363	1411	1681	2962	1712			
4	3024	3355	1411	1681	2962	1650	771		
5	3078	3309	1411	1681	2962	1697		3349	1257
6	3085	3363	1411	1681	2962	1681			

Table (1) infrared spectrum data for imidazolidn-4-one derivatives compounds (1,2,3,4,5,6)

Synthesise of compounds(7,8,9,10) by react between schiff base (3-6) with chloro acetyl chloride.

compound (7) 1-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-3-chloro-4- (4-(3-chloro-2- (4-(dimethylamino) phenyl) -4-oxoazetidin-1-yl) phenyl)-4-methyl azetidin -2- one was obtained by react between schiff base (3) with chloro acetyl chloride to get (7) as white solid, yield 41.8%, Rf =0.45, M.P(255)°C.

compound (8) 1-(4-(1H-benzo [d] imidazol-2-yl)phenyl)-3-chloro-4-(4-(3-chloro-2-(4-chlorophenyl)- oxoazetidin-1-yl) phenyl) -4-methylazetidin-2-one was obtained by react between schiff base (4) with chloro acetyl chloride to get (8) as black solid yield 64.1%, Rf =0.65, M.P(155d.) OC.

compound (9) 1-(4-(1H- benzo[d] imidazol-2-yl)phenyl)-3-chloro-4-(4-(3-chloro -2-(4 – hydroxy -3-methoxyphenyl)

-4-oxoazetidin-1-yl) phenyl) -4-methyl azetidin -2-one was obtained by react between schiff base (5) with chloro acetyl chloride to get (9) as purple solid yield 50.8%, Rf =0.7, M.P(188d.) 0 C.

compound (10) 1-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-3-chloro-4-(4-(3-chloro -2-oxo-4 -phenylazetidin-1-yl) phenyl) -4-methylazetidin-2-one was obtained by react between schiff base (6) with chloro acetyl chloride to get (10) as purple solid yield 64.1%, Rf =0.72, M.P(148d.)°C.

The infrared spectrum data of compound (7,8,9,10) show absorption at $(2909-2977)\text{cm}^{-1}$ for(Ar-H),(32243440)cm⁻¹ (N-H),(1396-1411)cm⁻¹ (C-N),(1696)cm⁻¹ (C=N),and show band at (2947-2970) cm⁻¹ for (C-H)CH₃, and (1696-1681) cm⁻¹ for(C=O)(β - lactam) compound (11)show band at (771)for(C-Cl) compound(15)showband at(3346) cm⁻¹ for OH, (1065) cm⁻¹ (C-O) Ph-O-CH₃⁽¹⁹⁾

Comp	υAr-H	υN-H	υC-N	υC=N	υC-H	υС=Οβ	υC-Cl	υΟΗ	υArOCH ₃
	aromatic				aleph	Lactam			
7	3008	3440	1396	1696	2947	1681			
8	3008	3355	1411	1598	2947	1697	771		
9	3055	3224	1396	1596	2947	1650		3346	1265
10	3008	3363	1396	1596	2970	1697			

Table (2) infrared spectrum data for β-lactam derivatives compounds (7,8,9,10) cm⁻¹

Synthesise of compounds (11,12,13,14) by react between schiff base (3-6) with thioglycollic acid.

compound (12) 3-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-2-(4-(2-(4-chloro phenyl)-4-oxothiazolidin-3-yl) phenyl)-2-methylthiazolidin-4-one obtained by react between schiff base (4) with thioglycollic acid to get (12) as brown seram, Rf = 0.52.

compound (13) 3-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-2-(4- (2-(4- hydroxy -3- methoxyphenyl)-4-oxothiazolidin-3-yl) phenyl)-2-methylthiazolidin-4-one obtained by react between schiff base (5) with thioglycollic acid to get (13) as brown seram ,Rf =0.71.

compound (14) 3-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-2-methyl-2-(4- (4- oxo -2- phenylthiazolidin-3-yl)phenyl)thiazolidin-4-one obtained by react between schiff base (6) with thioglycollic acid to get (14) as brown seram, Rf = 0.499.

Synthesis compound

(15,16,17,18,19,20,21,22) obtained by react schiff base (3-6) with α -amino acid

compound (15) 3-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-2-(4-(2-(4-(dimethy lamino) phenyl)-5-oxoimidazolidin-1-yl)phenyl)-2-methylimidazolidin-4-one was obtained by react between schiff base (3) with glycine to get (15) as brown solid, yield 71..43%, Rf=0.45, M.P(170d.)°C.

compound (16) 3- (4-(1H-benzo [d] imidazol-2-yl) phenyl) -2-(4-(2-(4-chlorophenyl) -5-oxoimidazolidin-1-yl) phenyl)-2-methylimidazolidin-4-one was obtained by react between schiff base (4) with glycine to get (16) as black solid, yield 58.61%, Rf =0.58 , M.P(147d.)°C

compound (17) 3-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-2-(4-(2-(4-hydroxy -3- methoxy phenyl)-5-oxoimidazolidin-1-yl) phenyl)-2-methylimidazolidin-4-one was obtained by react between schiff base (5) with glycine to get (17) as purple solid, yield 90.46%, Rf=0.61, M.P(168d.)^OC.

compound (18) 3-(4-(1H-benzo [d]imidazol-2-yl) phenyl) -2-methyl-2-(4-(5-oxo-2-phenyl) imidazolidin-1-yl) phenyl)imidazolidin -4-one was obtained

by react between schiff base (6) with glycine to get (18) as brownrod solid, yield 90.1% , Rf =0.69 , M.P(173) $^{\circ}$ C . The 1 H-NMR(CDCl₃) spectrum data of compound (18) show δ :6.87-8.3(m , 17H , Ar-H) , 5 (s , 1H , NH) , 3.54-3.44 (m , 2H,CH) , 2.3 (m,3H,NH) ,1.5(s,3H,CH₃), 6.1(m,1H,CH).

compound (19) 3-(4-(1H-benzo [d] imidazol-2-yl) phenyl) -2-(4-(2-(4-(dimethyl amino) phenyl) -4-methyl-5oxoimidazolidin-1-yl) phenyl)-2,5--4-one imidazolidin dimethyl obtained by react between schiff base (3) with alanine to get (19) as brown solid, yield 96.23%, Rf = 0.53, M.P(149d.) C. The ¹H-NMR (CDCl₃) spectrum data of compound (19) show δ : 6.3-8.2 (m,17H, Ar-H), 1.2 (s,6H,CH₃), 4.5 $(s,1H,NH),3.7(m,2H,CH),1.69(s,3H,CH_3)$ $,3.2(m,6H,CH_3).$

compound (20) 3-(4-(1H-benzo[d]imidazol-2-yl)phenyl) -2-(4- (2-(4-chloro phenyl) -4- methyl -5-oxoimidazolidin-1-yl) phenyl)-2,5-dimethyl imidazolidin-4-one was obtained by react between schiff base (4) with alanine to get (20) as brown solid, yield 89.49%, Rf=0.64, M.P(179)°C.

compound (21) 3-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-2- (4-(2-(4-hydroxy-3-methoxy phenyl) -4-

methyl-5-oxoimidazolidin-1-yl)phenyl) - 2,5- dimethy limidazolidin -4- one was obtained by react between schiff base (5) with alanine to get (21) as purple solid, yield 97.8%, Rf =0.71, M.P(185)°C.

compound (22) 3-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-2,5-dimethyl-2- (4-(4-methyl -5-oxo-2-phenylimidazolidin -1-yl) phenyl) imidazolidin-4-one was obtained by react between schiff base (6) with alanine to get (22) as brown solid, yield 84.345%, Rf=0.62 . M.P(155) C.

The 1 H-NMR (CDCl₃) spectrum data of compound (22) show δ : 7.2-8.3 (m , 17H , Ar-H) , 5.1 (s , 1H , NH) , 3.7 (m , 2H , CH) , 1.28 (m,6H ,CH₃) , 2(s,2H,NH), 6.4(m,1H,CH).

The infrared spectrum data of (15,16,17,81,19,20,21,22)compound show absorption at (3024-3085)cm⁻¹ for (Ar-H),(3309-3456) cm⁻¹ (N-H), (1396-1411)cm⁻¹ (C-N), (1504-1598)cm⁻ ¹(C=N), and show band at(2838-2985)cm⁻ ¹for (C-H)CH₃, and(1681-1712) cm⁻¹ for(C=O), compound (13) and (14) show band (825)for at (C-Cl), compound(17)showband at(3749) cm⁻¹ for OH ,(1257) cm⁻¹ (C-O) Ph-O-CH₃, but compound (18) show band at (3347) cm⁻¹ for OH ,(1265) cm⁻¹ (C-O) Ph-O-CH₃ (20)

Table (3) infrared spectrum data for imidazolidn-4-one derivatives compounds $(15,\!16,\!17,\!18,\!19,\!20,\!21,\!22)~cm^{-1}$

Comp.	υAr-H	υN-H	υC-N	υC=N	υС-Н	υC=O	υC-Cl	υОН	υArOCH ₃
					aleph.				CO
15	3055	3456	1396	1596	2838	1697			
16	3055	3384	1404	1504	2838	1697	825		
17	3055	3350	1411	1589	2838	1712		3349	1257
18	3024	3363	1411	1596	2838	1650			
19	3078	3309	1411	1596	2931	1697			
20	3085	3355	1411	1598	2985	1681	825		
21	3070	3309	1411	1596	2949	1681		3346	1265
22	3070	3363	1411	1596	2931	1681			

Table(4):- Analytical and physical data of compounds .

No.	Molecular formula	Color	M.P°C	Yield%	R_{f}
1	C ₁₃ H ₁₁ N ₃ (209.247)	silver	211	76.92	0.34
2	C ₂₁ H ₁₈ N ₄ (326.394)	purple	220.	941	0.64
3	C ₃₀ H ₂₇ N ₅ (457.569)	orang	240	92.28	0.62
4	C ₂₈ H ₂₁ N ₄ Cl (448.946)	Brown	140 d.	20.79	0.375
5	C ₂₉ H ₂₄ N ₄ O ₂ (469.190)	orang	163d.	46.1	0.2
6	$C_{28}H_{22}N_4$ (414.501)	Goldenrod	153d.	27.96	0.43
7	C ₃₄ H ₂₉ N ₅ O ₂ Cl ₂ (610.532)	white	255	41.8	0.45
8	C ₃₂ H ₂₃ N ₄ O ₂ Cl ₃ (601.910)	black	155	64.1	0.65
9	C ₃₃ H ₂₆ N ₄ O ₄ Cl ₂ (591.102)	purple	180d	50.8	0.7
10	C ₃₂ H ₂₄ N ₄ O ₂ Cl ₂ (567.469)	purple	148	40.56	0.72
11	$\begin{array}{c} C_{34}H_{31}N_5O_2S_2\\ (605.722) \end{array}$	Brown	liquid	88	0.21
12	C ₃₂ H ₂₅ N ₄ O ₂ S ₂ Cl (605.722)	Brown	liquid	92	0.52
13	C ₃₃ H ₂₈ N ₄ O ₄ S ₂ (608.730)	Brown	liquid	77.7	0.71

14	C ₃₃ H ₂₆ N ₄ O ₂ S ₂ (562.704)	Brown	liquid	93	0.499
15	$C_{34}H_{33}N_7O_2$ (571.672)	Brown	170 d.	76.45	0.45
16	$C_{32}H_{27}N_6O_2C1$ (563.049)	black	147	58.614	058
17	$C_{33}H_{30}N_6O_4$ (574.629)	purple	168	90.46	0.61
18	$C_{32}H_{28}N_6O_2$ (528.604)	brownrod	173	90.1	0.69
19	$C_{36}H_{37}N_7O_2$ (571.672)	Brown	149d.	96.23	0.53
20	$C_{34}H_{31}N_6O_2C1$ (591.102)	Brown	179	89.49	0.64
21	C ₃₅ H ₃₄ N ₆ O ₄ (574.629)	purple	185	97.8	0.71
22	$C_{34}H_{32}N_6O_2$ (556.657)	brownrod	155	84.345	0.62

References

- 1- Shadia A. Galala, Ahmed S. Abdelsamiea, Mireya L. Rodriguezb, Sean M. Kerwinb and Hoda I. El Diwania; *Eur J Chem*, 2010, (2), 67-72
- 2-Bhatnagar A., Sharma P. K, Kumar N. *International J. PharmTech Research*, 2011, 3, (1), 268-282.
- 3-Minaxi Maru1 and M. K. Shah, Journal of Chemical and Pharmaceutical Research, 2012, 4(3):1638-1643
- **4-** Anshul Chawla, Ashu Sharma and ,Anil kumar Sharma,*Der Pharma Chemica*, 2012, **4 (1):**116-140
- **5-** Paloma Liras Juan F. Martín, *J.Internatonal microbiology* , 2006; 9-19
- 6-Hans Emtenals, Gabe Soto, Scott J. Hultgren, Garland R. Marshall, and Fredrik Almqvist; *organic letters*, 2000, **2**, **(14)**, 2065-2067.
- 7-Fekade Bruck Sime, Michael S Roberts, Sandra L Peake, Jeffrey Lipman and Jason A Roberts, Sime et al. Annals of Intensive Care 2012, 2:35

- 8- Lan-Ying Qin a, Andrew G. Cole a, Axel Metzger a, Linda O'Brien a, Xiling Sun b, Jin Wub, Yan Xu b, Kai Xu b, Ying Zhang b, Ian Henderson, *J.Tetrahedron letters*, 2009,50419-422.
- **9-** A. Jamal Abdul Nasser, A.Idhayadhulla,R.Surendra Kumar and J. Selvin. *J* of chem., 2010, 7, 1320-1325.
- **10-** G. Omprakash, Y. Ananeyulu, N. Siva Subrama,ian, M. Ramadevl and G. Vijaylakshmi, *Int,J,Chem.Sci*; 2010, **8(2)**, 783-790.
- **11-** A.Albert; "hetrocyclic chemistry"; Athlone press London, 1959.
- **12-** G.F.Dutfin ;" Adv.Hetrocyclic chem ." ,3,19 (1964).
- 13-SADAF J. GILANI, SUROOR A. KHAN, OZAIR ALAM, VIJENDER SINGH and ALKA AROR ,*J. Serb. Chem. Soc.*, 2011, 76 (8), S1–S9.
- 14-Cherkupally Sanjeeva Reddy,1,*
 Gaddam Rajesh Kumar,1, Macherla
 Vani Devil and Adki Nagaraj2,*Acta Chim. Slov.* 2011, 58, 576–581

- **15**-Arvind k. Singh, Geeta Mishra and Kshitiz Jyoti *Journal of Applied Pharmaceutical*
 - Science, 2011, **01 (05)**; 44-49
- **16**-G. Nagalakshmi*, T. K. Maity and B. C. Maiti, *Pharmacologyonline*, 2011, **1**: 1228-1246.
- 17- Panneer Selvam, T, P. P. Radhika1, S. Janagaraj1, A. Siva Kumar;
 Researchin Biotchnology, 2011, 2
 (3),50-57.
- 18- Bhushan Baviskar, Bhagyesh Baviskar, Suvarna Chuadhary, Kanchan Parwani, Pinky Balani, Vikrant Salode, Shailesh Patil and S. S.

- Khadabadi; *J. Chem.*, 2009, **2,(1)**, 186-190,6.
- **19-** N. B. Colthup, L. H. Daly,and S.E. Wiberely;"Introduction to infrared and raman spectroscopy" 2nd Ed. Academic Press .Inc.J.R.Dyer;(1975)
- 20- Maira GR Pitta, Andréa CA Silva, Juliana Kelle AL Neves, Poliana G Silva, João I Irmão, Elizabeth Malagueño, José V Santana, Maria CA Lima, Suely L Galdino, Ivan R Pitta, Mônica CPA Albuquerque, mentinst oswaldo cruz, Riode janeiro, 101,2006 (supp1.1);313-316.