Synthesis of different heterocyclic compounds derived from some amino acids

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Abstract:

Some of heterocyclic compounds have been synthesized using some amino acids as a starting materials provides that the synthesized products bear parts of the amino acids structure. The types of these compounds are pyrazoles, pyridazines, thiazepines, and oxazepines. A preliminary test to evaluate the antimicrobial potency of some of the synthesized compounds were carried out using two types of organisms (+ve) and (-ve). The tests demonstrated an encouraging results for a good number of the tested compounds.

1-Introduction

The synthesis of heterocyclic compounds has received a considerable attention because of the different types of these compounds have various applications such as in pharmaceutical, agrochemical and industry[1-5]. Some of these compounds displayed wide spectrum of activities such as antibacterial, anti-inflammatory, antidepressant, antihistaminic, anticonvulsant and other activity[6-12].

A various procedures for the synthesis of different heterocyclic derivatives were developed including those for pyrazoles , pyridazines, thiazepines and oxazepinZes[13-25] . The derivatives of these types have various substituents in order to estabilish a conclusion reflects the chemical structure – biological activity relationship.

The coal of this work is to synthesis some new heteroyclic derivatives incorporated in their structures a substantial part of different amino acids. The synthesis of these compounds requires the convertion the amino a acids into it is hydrazides, Acid chlorides,thioureas and shiff- bases.

2-Experimental

Melting points were recorded using SMP 30 melting point instrument (Stuart, Germany), and they are uncorrected. ^{1}H nmr spectra were recorded in DMSO-d_6 on Bruker(400 MH_Z) DMX-500 NMR spectrophotometer, at Al- albayt university , Jordan. The chemical shifts were recorded as values

in ppm using tetramethyl silane (TMS) as internal standerd. FT-IR spectra were recorded as KBr discs on Shimadzu FT-IR 8400S spectrophotometer .All reactions and the purity of the synthesised compounds were monitored by using TLC (silica gel).

Synthesis of amino acids esters (E_1-E_5)

In a round bottom flask, a solution of amino acid (0.003 mole) in absolute ethanol (40 ml) was placed in ice -bath and thionyl chloride (3.3 ml, 0.45 mole) was added dropwise . The reactant was left to stirr for 30 minutes at room temperature , then heated by reflux for 3 hours. The solvent was removd by rotary evaporator, table(1).

Synthesis of amino acid hydrazides(H_1-H_5)

To amino acid ester(0.02 mole) in absolute ethanol (40 ml), hydrazine hydrate(80%) (0.03 mole) was added . The reaction mixture was heated by reflux for 10 hours , followed by removal of solvent using rotary evaporator under vacuum. The residue was recrystallized from ethanol, table(2).

Synthesis of pyrazoles (P_1-P_7)

Ethyl acetoacetate (0.025 mole) contained acetic acid (0.5 ml) was added to a solution of amino acids hydrazides(H_1-H_5)(0.025 mole) in absolute ethanol(50 ml). The reaction mixture was heated by reflux for 7 hours . The solvent was removed using rotary evaporator under vacuum and the residue was washed with sodium carbonate solution. The product was filtered, dried and recrystallized from ethanol, table(3)

Synthesis of pyridazines (A_1-A_4)

A solution of phthalic anhydride(0.001 mole) in acetic acid(20 ml) was added slowly to a solution of amino acid hydrazides(H_1-H_5) (0.001 mole) in ethanol (30 ml). The reaction mixture was heated by reflux for 8 hours. The crude product was poured into ice –bath and a solution of sodium bicarbonate was added with stirring until solution turns neutral. The product was filtred, washed with distilled water, dried and recrystallized from ethanol, table(4).

Synthesis of protected phenyl alanine

Phenyl alanine (5 g, 0.03 mole) was dissolved in sodium hydroxide solution (22.5 ml, 2N). A solution of p-methoxybenzoyl chloride (5.1 g, 0.03 mole) in sodium hydroxide solution (69 ml, 2N) was added dropwise with stirring at room temperature. The stirring was continued for additional 30 minutes, followed by neutralization of the product by addition of hydrochloric acid until pH= 6 . The resulted precipitate was washed with

distilled water few times . The product was dried, recrystallized from ethanol, gave white crystals, m.p. 240-242^{o} C, 91% .

Synthesis of acid chloride of amino acids (B_1, B_2)

Thionyl chloride (1.1 ml, 0.015 mole) was added dropwise with stirring to a cooled solution of amino acid (1.15 g, 0.01 mole)prolin or (2.99 g, 0.01 mole) phenylalanine in dichloromethane (30 ml). The reactants were left to stirr at room temperature for 30 minutes, then heated by reflux for 3 hours. The solvent was removed under vacuum to produce a grey oil, table (5).

Synthesis of thiourea derivatives (u_1-u_5)

A solution of acid chloride of amino acid (o.o25 mole) in acetone (30 ml) was added dropwise with stirring to solution of potassium thiocyanate (2.42 g, 0.025 mole) in acetone (30 ml). The reactants were heated by reflux for 30 minutes. The resulted product was cooled to room temperature and a solution of primary amine (0.025 mole) in acetone (30 ml) was added with stirring at room temperature for 2 hours. Hydrochloric acid (100 ml, 0.1 N) was added to the product. The resulted precipitate was filtered, washed with distilled water and recrystallized from chloroform or THF, table(6).

Synthesis of thiazepine derivatives (Z_1-Z_5)

Sodium hydride (60% on mineral oil)(0.4 g,0.006 mole) was added gradually to solution of thiourea derivative (o.006 mole) in dimethylformamide(DMF) (50 ml) with continuous stirring at room temperature. After the evolution of the hydrogen was seized, 1,4-dibromobutane (1 ml, 0.009 mole) was added dropwise with stirring. The reactants were left to stir for 6 hours at room temperature followed by solvent removal using rotary evaporator under reduced pressure. The residue was recrystallizd from THF, table(7).

Synthesis of Schiff-bases of amino acids esters (S_1-S_7)

A solution of aldehyde (0.005 mole) in absolute ethanol(20 ml) was added gradually with stirring to round bottom flask contained solution of amino acid ester (E_1-E_5) (0.005 mole) in absolute ethanol (30 ml) . The reactants were heated by reflux for 6 houres . The solvent was removed by rotary evaporator under vacuum and the residue was recrystallized from absolute ethanol, table(8).

Synthesis of 1,3-oxazepine derivatives (O_1-O_7)

A solution of Schiff base (0.003 mole) in dry benzene (25 ml) was placed in round bottom flask, and phathalic anhydride (0.003 mole) was added gradually. The reactants were heated by reflux for 8 hours, then the

solvent was removed by rotary evaporator under vacuum. The residue was recrystallized from absolute ethanol, table(9).

3-Results and discussion

In order to synthesized a new heterocyclic compounds of different types and ring size, some important intermediate compounds were synthesized successively. The hydrazides of some amino acids (H_1-H_5) were synthesized and used in synthesizing two types of pyrazoles. The first type was resulted from the reaction of the mentioned hydrazid with acetyl acetone in presence of glacial acetic acid (P_1-P_3). The second type(P_4-P_6) was a result of the reaction of the synthesized hydrazides with ethyl acetoacetate under the same conditions.(scheme 1). The chemical structure of the synthesized pyrazoles was elucidated by spectroscopic methods. The FTIR of the derivatives showed a stretching vibration of cyclic and non-cyclic carbonyl groups between 1664-1685 cm^{-1} , in addition to stretching absorption bands at 1600-1624 cm^{-1} and 3180-3371 cm^{-1} belongs to C=N and NH_2 groups respectively,(table 3). The ^{1}Hnmr spectra of pyrazoles P_4 and P_5 were in agreement with their structure,(table 10).

The hydrazides (H^1-H^5) were also used to synthesis pyridazine derivatives (A_1-A_4) by reaction with phathalic anhydride in acidic medium (schem 1). The reaction starts with nuclophlic attack on one of the carbonyl groups of phathlic anhydride by lone pair of electron located on hydrazide amino group. This attack was followed by ring closure resulted in formation of six-membered ring heterocyclic derivatives (pyridazine derivatives). The IR absorption bands of these derivatives appeared at 1620 -1710 cm^{-1} were attributed to cyclic and non – cyclic carbonyl groups and those for NH and NH_2 groups appeared at 3128 – 3369 cm^{-1} . The values for other groups are listed in table (4). The ^{1}Hnmr spectra of compound A_1 is in agreament with proposed structure and the position of the signals are listed in table (10). The mentioned reactions were represented in scheme(1).

Thiazepine derivatives (Z_1 – Z_5) were synthesized from the reaction of some thiourea derivatives with 1,4-dibromobutane in presence of potassium hydride ,scheme (2). The thioureas were derived from the reaction of acid chloride of some amino acids with potassium thiocyanate ,followed by couplling with primary amines. The resulted thiazepines showed absorption bands at 1641 – 1666 cm^{-1} attributed to the stretching vibration of imine (C=N) groups in IR spectra. The bands at 1671 – 1708 cm^{-1} are due to amidic carbonyl groups, table (7). The ^{1}Hnmr spectra of thiazepine derivatives Z_1,Z_3,Z_5 confirmed their structures, table (10).

Finally, some benzoxazepines (O_1-O_7) were synthesized from nucleophilic reaction of Schiff- bases, derived from some amino acid esters, with phathalic anhydride. The reaction included the formation of (2+5) intermediate via pericyclic mechanism, schem (3) . The IR spectra of the products showed absorption bands of lactam carbonyl groups at 1635 – 1724 cm^{-1} , whil those belong to lactone carbonyl absorption appeared at 1770 – 1795 cm^{-1}. The carbonyl ester groups of these compounds showed absorption bands were at 1728-1741 cm^{-1} , table (9). The ^{1}Hnmr spectrum of compound O_4 confirmed it is structure, (table 10).

Antimicrobial activity test

Some of the synthesized compounds were tested against two types of bacteria, staphylococcus(+ve) and Acientobacter(-ve). Two concentrations of the tested compounds were , 0.02 g/ml and 0.0002 g/ml. The most potent compounds against the growth of the used bacteria are A_3, O_4, U_1, Z_1, Z_2,, P_4, P_5, and table (11) summarized the results of the tested compounds. Adeatailed study may be necessary to make a comprehensive evaluation to the synthesized compounds.

Table (1) : Physical and spectral data of synthesized amino acids esters(E_1 – E_2)

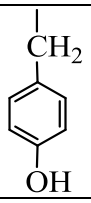
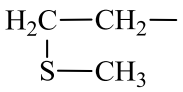
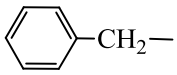
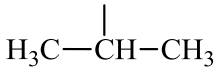
AComp No.	R	ppm°	color	yelid	υ(C=O) cm^{-1}	υ(NH_2) cm^{-1}	υ(C=C)Ar cm^{-1}	υ(C-H) Ar cm^{-1}	υ(C-H) Alph cm^{-1}
E_1	H——	100-98	white	90	1739	3466	1595	3070	2991,2843
E_2		125-123	white	92.4	1743	3408	1581	3037	2985,2872
E_3		130-127	white	88	1747	3479	-	-	2976, 2881
E_4		166-163	white	91.5	1739	4319	-	-	2964,2893
E_5		138-135	white	85.4	1734	3456	-	-	2966, 2875

Table (2) : Physical and spectral data of synthesized amino acids hydrazides($H_1 - H_6$)

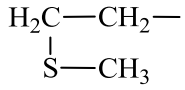
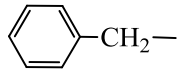
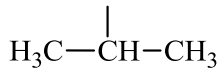
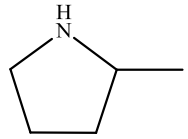
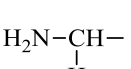
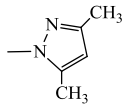
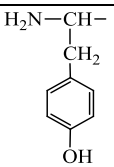
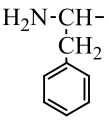
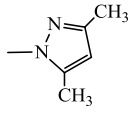
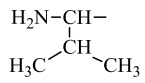
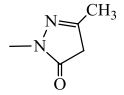
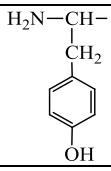
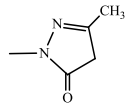
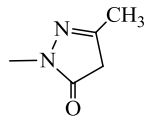
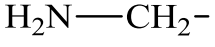
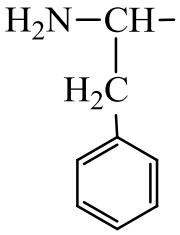
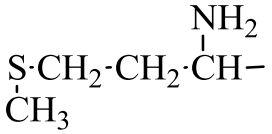
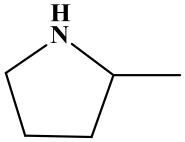
Comp No	R	ppm	color	yelid	υ(C=O) cm^{-1}	υ($NHNH_2$) cm^{-1}	υ(C=C)Ar cm^{-1}	υ(C-H) Ar cm^{-1}	υ(C-H) Alph cm^{-1}
H_1		oily	white	83.3	1631	3244,3142	1577	3034	2980,2891
H_2		=	white	86.4	1635	3338,3207	1593	3022	2920
H_3		73-71	white	92	1618	3284,3153	-	-	2951,2895
H_4		92-89	white	75.7	1614	3280,3180	-	-	2985,2864
H_5		69-67	white	79	1612	3252,3146	-	-	2951,2887
H_6		oily	white	٧٨	1637	3253	-	-	2953,2884

Table (3) : Physical and spectral data of synthesized pyrazoles($P_1 - P_6$)

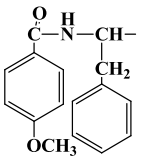
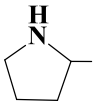
Comp No.	R_1	R_2	ppm	color	yiled	υ(C=O) cm^{-1}	υ(NH_2) cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) Ar cm^{-1}	υ(C-H) Ar cm^{-1}	υ(C-H) Alph cm^{-1}
P_1			202-200	white	69.3	1685	3371	1624	-	-	2999
P_2		=	193-191	white	71	1664	3180	1612	1545, 1515	3041	2976
P_3			175-173	white	52	1678	3298	1612	1568, 1519	3064	2980, 2874

P_4			**196-195**	**white**	**54.5**	**1681**	**3338**	**1600**	**-**	**-**	**2966, 2877**
P_5			**193-190**	**white**	**76**	**1687**	**3302**	**1614**	**1572, 1541**	**3045**	**2926**
P_6			**219-217**	**white**	**48**	**1678**	**3298**	**1612**	**-**	**-**	**2980, 2806**

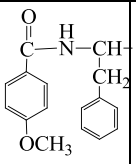
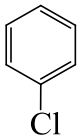
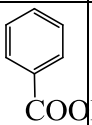
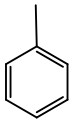
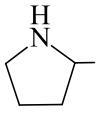
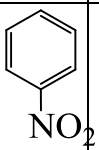
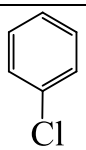
Table(4) : Physical and spectral datad of synthesized pyridazines(A_1 _ A_4)

Comp No.	**R**	**ppm**	**color**	**yiled**	**υ(C=O) cm^{-1}**	**υ(NH_2) cm^{-1}**	**υ(NH) cm^{-1}**	**υ(C=C) cm^{-1}Ar**	**υ(C-H) Ar cm^{-1}**	**υ(C-H) Alph cm^{-1}**
A_1		**151-179**	**white**	**80.6**	**1678,1627**	**3298**	**3198**	**1577**	**3055**	**2916**
A_2		**176-174**	**white**	**67.7**	**1710**	**3192**	**3379**	**1568**	**3063**	**2999**
A_3		**115-113**	**white**	**84.6**	**1662**	**3271**	**3128**	**1600**	**3028**	**2985**
A_4		**143-142**	**white**	**56.8**	**1645,1620**	**3369**	**3178**	**1533**	**3043**	**2974, 2821**

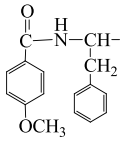
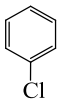
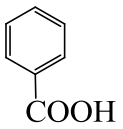
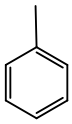
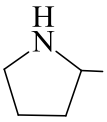
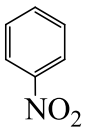
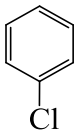
Table(5) : Physical and spectral data of synthesized amino acids acid chlorides (B_1 and B_2)

Comp No.	R	ppm	color	yiled	υ(C=O) cm^{-1}	υ(N-H) cm^{-1}	υ(C=C)Ar cm^{-1},	υ(C-H) Arcm^{-1}	υ(C-H) Alph cm^{-1}
B_1		oily	brown	83	1788	3300	1595	3056	2984, 2867
B_2		=	=	76	1787,	3396	–	–	2983, 2884

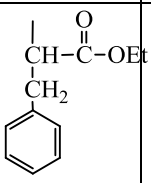
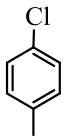
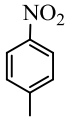
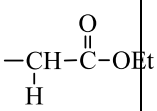
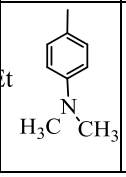
Table(6) : Physical and spectral data of synthesized amino acids thiourea($U_1 – U_5$)

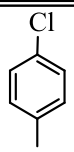
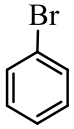
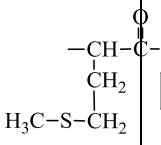
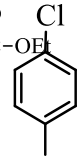
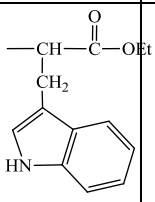
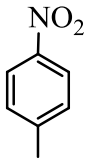
Comp No.	R_1	R_2	ppm	color	yiled	υ(C=O) cm^{-1}	υ(N-H) cm^{-1}	υ(C=S) cm^{-1}	υ(C=C) Ar cm^{-1}	υ(C-H) Ar cm^{-1}	υ(C-H) Alph cm^{-1}	υ(Otheres) cm^{-1}
U_1			172-171	yellow	90	1664	3392	1176	1593	3030	2941	υ(C-Cl) 823
U_2	=		185-183	white	76.4	1681	3338, 3275	1170	1599	3044	2976, 2841	υ(C-OH) 3410
U_3	=		147-145	brown	68	1683	3284	1174	1578	3015	2970, 2837	-
U_4			202-200·	yellow	87.8	1669	3410, 3192	1166	1600, 1496	3059	2933, 2839	υ(C-OH) 3423
U_5	=		146-143	yellow	80	1693	3171	1213	1585	3020	2970, 2858	υ(C-Cl) 806

Table(7) : Physical and spectral data of synthesized thiazepines($Z_1 - Z_5$)

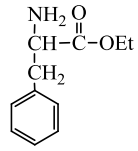
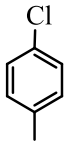
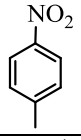
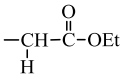
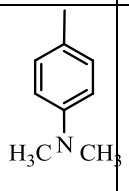
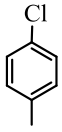
Comp No.	R_1	R_2	ppm	color	yelid (%)	υ(C=N) cm^{-1}	υ(C=O) cm^{-1}	υ(NH) cm^{-1}	υ(C=C) Ar cm^{-1}	υ(C-H) Ar cm^{-1}	υ(C-H) Alph cm^{-1}	υ(Otheres) cm^{-1}
Z_1			201-200	brown	65.6	1656	1685	3338	1602	3053	2983,2885	(C-Cl) 823
Z_2	=		193-191	white	54	1660	1701	3234	1606	3036	2968	υ(C-OH) 3400
Z_3	=		123-121	brown	52	1650	1671	3354	1577	3030	2943,2843	
Z_4			196-195	yellow	76.4	1641	1691	3217	1602	3010	2970	υ(C-OH) 3448
Z_5	=		89-87	yellow	65.3	1666	1708	3167	1600	3051	2955	C-Cl)(υ 763

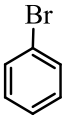
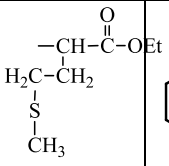
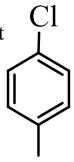
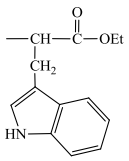
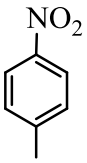
Table(8) : Physical and spectral data of synthesized amino acids shiff-bases(S_1-S_7)

Comp No.	R_1	R_2	ppm	color	yiled	υ(C=O) cm^{-1}	υ(C=N) cm^{-1}	υ(C=C)Ar cm^{-1}	υ(C-H) Ar cm^{-1}	υ(C-H) Alph cm^{-1}	υ(Otheres) cm^{-1}
S_1			204-202	yellow	76.4	1737	1629	1597, 1494	3061	2982, 2870	υ(C-Cl) 700
S_2	=		187-184	yellow	68	1739	1651	1602, 1485	3034	2974, 2881	υ(NO_2) 1521, 1346
S_3			195-193	yellow	71.8	1745	1654	1577	3016	2976	

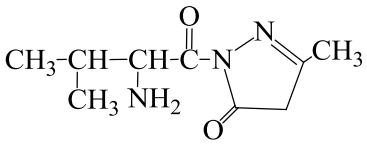
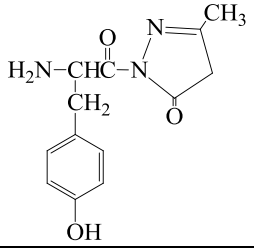
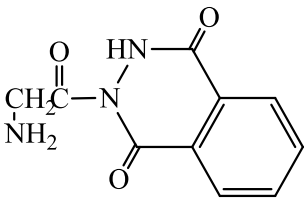
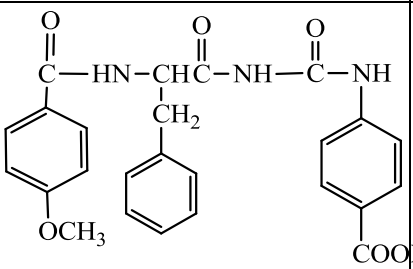
S_4	=		**oily**	**brown**	**81**	**1747**	**1649**	**1583**	**3034**	**2978**	**υ(C-Cl) 744**
S_5	=		**186-184**	**yellow**	**78.2**	**1747**	**1616**	**1585,**	**3068**	**2978, 2874**	**υ(C-Br) 810**
S_6			**176-174**	**yellow**	**73.7**	**1747**	**1660**	**1577**	**3036**	**2999, 2875**	**υ(C-Cl) 727**
S_7			**238-246**	**yellow**	**70**	**1759**	**1606**	**1577**	**3055**	**2983, 2862**	**υ(NO2) 1519, 1350,NH (3250)**

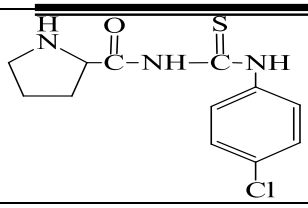
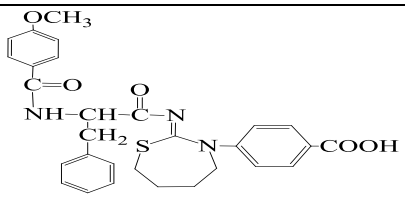
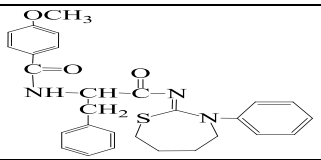
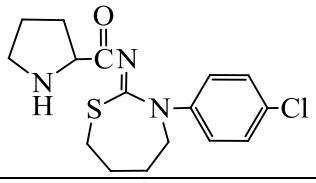
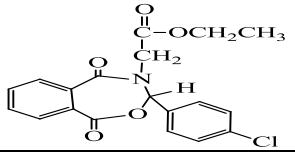
Table(9) : Physical and spectral data of synthesized oxazepines(O_1 _ O_7)

Comp No.	**R_1**	**R_2**	**ppm**	**color**	**yiled**	**υ(C=O) cm^{-1}ester**	**υ(C=O) cm^{-1} Lactone**	**υ(C=O) cm^{-1} Lactam**	**υ(C=C) Ar cm^{-1}**	**υ(C-H) Ar cm^{-1}**	**υ(C-H) Alph cm^{-1}**	**(Otheres) cm^{-1}**
O_1			**181-179**	**yellow**	**60**	**1739**	**1770**	**1649**	**1585**	**3084**	**2960, 2816**	**υ(C-Cl) 738**
O_2	=		**169-166**	**brown**	**55.8**	**1739**	**1786**	**1678**	**1600**	**3063**	**2983, 2874**	**υ(NO2) 1529, 1375**
O_3			**195-193**	**yellow**	**54.6**	**1728**	**1772**	**1635**	**1580**	**3041**	**2991**	
O_4	=		**oily**	**brown**	**73**	**1735**	**1768**	**1654**	**1600**	**3078**	**2939**	**υ(C-Cl) 840**

O_5	=		**184-182**	**yellow**	**75**	**1739**	**1772**	**1720**	**1570**	**3047**	**2987**	**υ(C-Br) 779**
O_6			**165-163**	**yellow**	**67**	**1741**	**1795**	**1703**	**1593**	**3063**	**2978,**	**υ(C-Cl) 715**
O_7			**193-191**	**yellow**	**69**	**1735**	**1795**	**1649**	**1582**	**3020**	**2955**	**υ(C-NO_2) 1516, 1336**

Table(10) : $^1H_{nmr}$ ($DMSO_{d6}$ ppm) data for some of the synthesized compounds

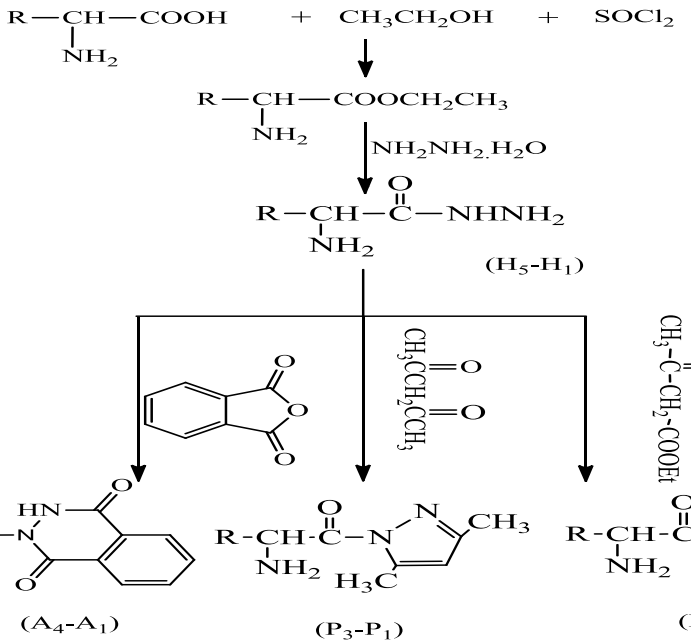
	1.1-1.3 (6H ,2xCH_3 ,d) 2.3 (3H ,=C-CH_3 ,S) ,2.4-2.6 (3H ,CH_2 (cyclic) and CH ,m) ,3.9-4.2 (1H ,H_2N-CH ,m) 6.1(2H ,NH_2 ,dd)
	1.15(3H,CH_3,S) , 1.90 (2H, CH_2, t) ,5.5 (2H ,NH_2 ,d) ,5.7 (^{1}H OH ,S) , ,6.5-7.2 (4H, Aromatics ,dd)
	2.1(2H,CH_2,S) ,5.2(2H,NH_2,S) ,6.4-8.2(5H.NHand 4Haromatics ,m)
	0.89 -1.01 (2H,CH_2,Cl) ,1.99-2.06 (1H,CH,t) ,3.40 (3H,OCH_3,S) ,5.21 S(2H,3×NH,S) ,8.00 -8.4 (12H,aromatics ,m

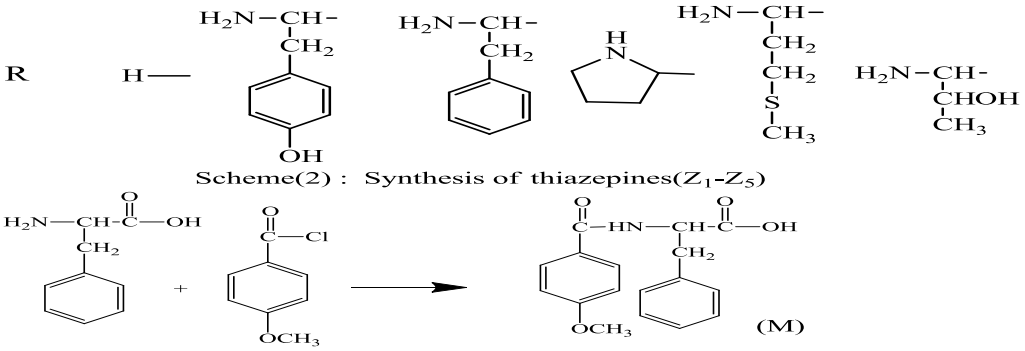
	1.1-1.2(4H ,2xCH_2 ,m) 1.5-1.6 (4H ,CH_2-NH-CH ,m), 4.9(1H,NCSNH ,S) ,7.1-7.7 (4H ,aromatics, dd),8.9 (1H ,CONH ,S) .
	3.1-3.3 (4H,2xCH_2thiazepine ring ,m) ,3.7-3.9 (9H, OCH_3 ,SCH_2 ,NCH_2,HN-CH-CH_2 ,t) 6.9-8.2 (13H ,aromatics ,m),8.7(1H ,NH ,S) ,10.9
	1.7-8.2 (13HxCH_2 cyclic,$CHCH_2$,m),2.1(1H,$CHCH_2$,t) 2.4 (2H,SCH_2,t) ,3.75(3H,OCH_3,S) ,3.8 (2H,NCH_2,m) ,6.8-8.4 (14H,NH and aromatics)
	1.9-2.1 (9H ,4H xCH_2 cyclic NH cyclic , m) ,3.4-3.6 (7H , NCH_2 and SCH_2 thiazepine ring , NCH_2 pyrrole ring ,CH ,m) ,6.5-8.2 (4H
	(3H ,CH_3,t) ,4.54-5.76 (2H,CH_2,m) ,(2H,CH_2,S),5.80 (1H ,CH (cyclic) ,s) ,8.28 -9.23 (8H aromatics ,m)

Table(11) : Antimicrobial activity data for some synthesized compounds

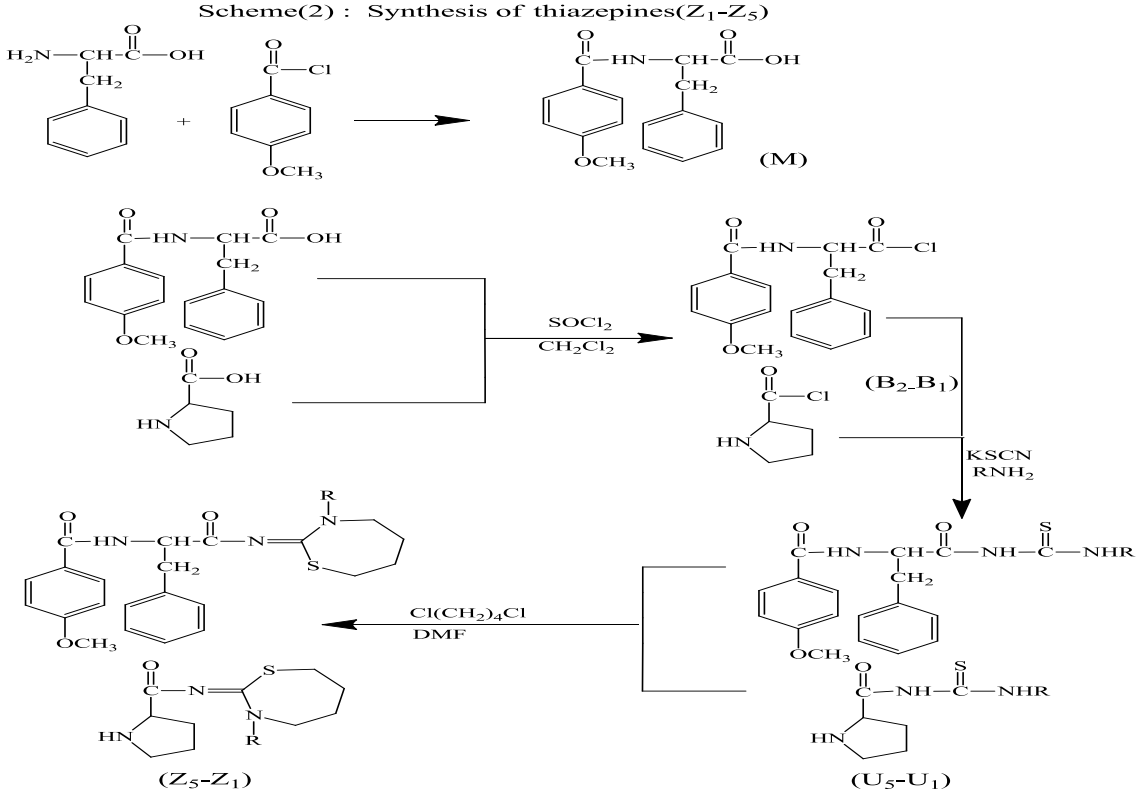
Comp No	staphylococcus (+ve)		Acientobacter (-ve)		comp No	staphylococcus (+ve)		Acientobacter (-ve)	
	0.02 g/ml	0.0002 g/ml	0.02 g/ml	0.0002 g/ml		0.02 g/ml	0.0002 g/ml	0.02 g/ml	0.0002/ g/ml
P_1	13	14	-	12	U_4	13	11	-	-
P_4	23	12	20	-	O_1	27	-	12	15
P_5	26	16	12	11	O_3	-	-	26	-
Z_1	22	20	12	20	O_4	25	-	10	-
Z_2	20	28	18	-	O_6	-	-	13	-
Z_5	-	13	30	12	S_2	-	-	-	-
U_1	21	10	-	10	S_7	-	10	23	12
A_1	14	12	19	13	A_3	23	12	12	10

Scheme(1) : Synthesis of pyrazoles(P_1-P_5), and pyridazines(A_1-A_4)

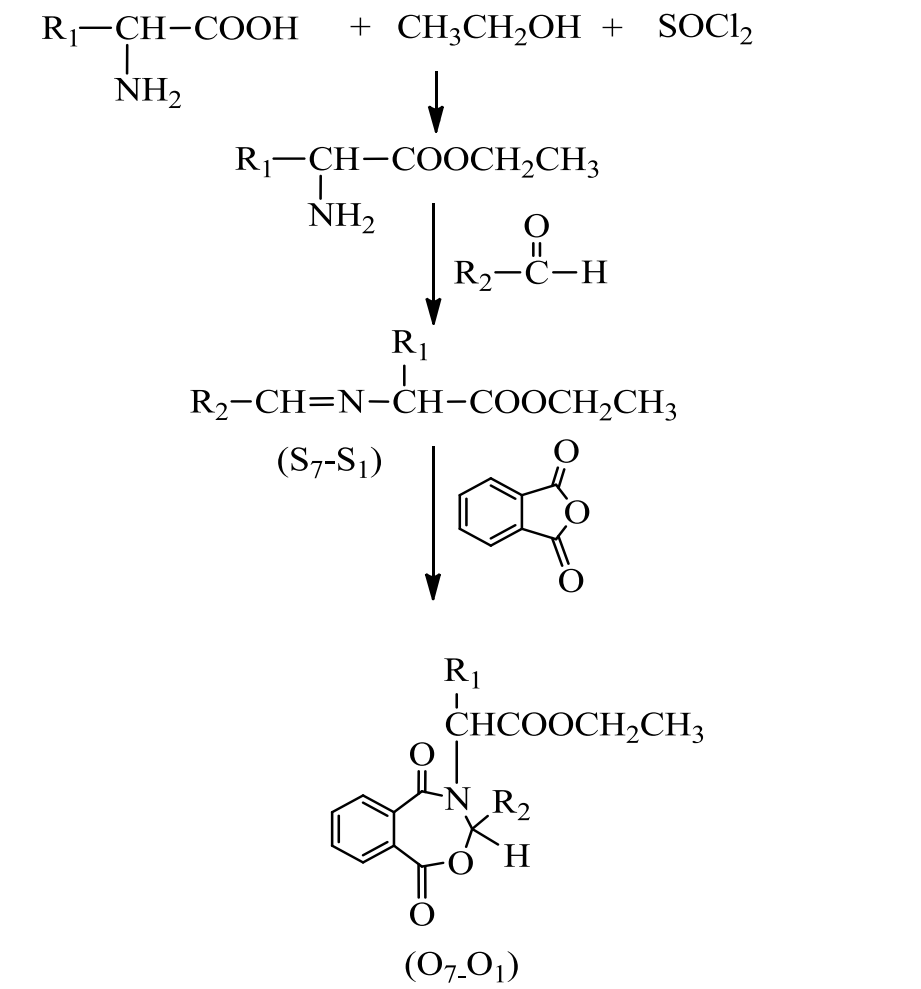


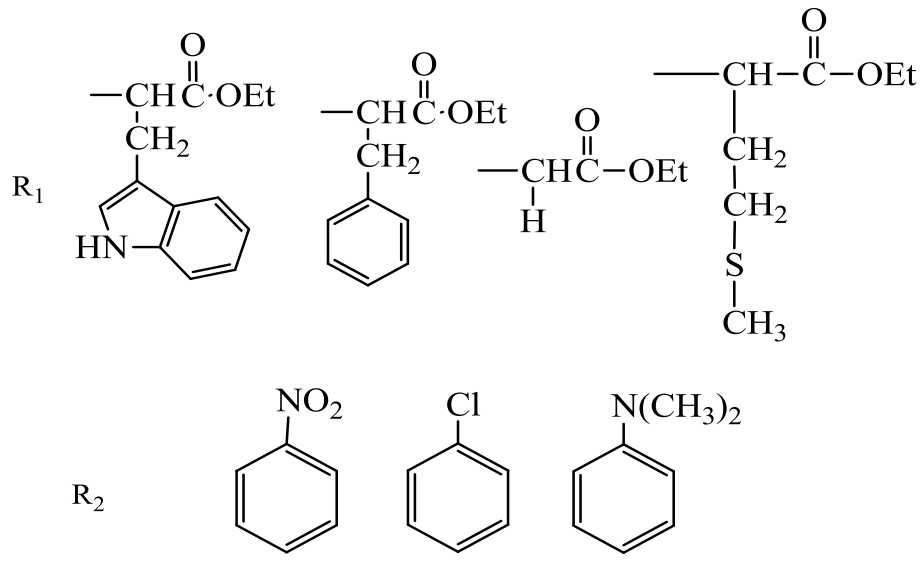


Scheme(2) : Synthesis of thiazepines(Z_1-Z_5)



Scheme(3) : Synthesis of oxazepines(O_1-O_7)





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الخلاصة

تم تحضير بعض المركبات الحلقية غير المتجانسة باستخدام الاحماض الامينية كمـــواد اولية بحيث تحتوي المركبات الناتجةعلى جزء من تركيـــب الحـــامض الامينـــي . والانـــواع المحضرة هي البايرزولات , البريدازينات , الثايوزبينات والاوكسازبينات . واجريت فحوصات اولية على بعض المركبات المحضرة لتقييم قوتها المضادة للبكتريا باستخدام نوعين من الاحياء المجهرية اظهرت هذه الفحوصات نتائج مشجعة لعدد جيد من المركبات تحت الاختبار.