Synthesis of Some Nitrogenous Heterocyclic Compounds and Their Fused Derivatives Derived From 8-Chloro-5-phenyl-pyrido[2,3-d]pyridazine

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الخلاصه

في هذه الدراسه ، تم تخليق(١٨)مركباتحتوي على حلقات ملتحمة غير متجانسة ،في المحور الاول تم تفاعل المركب ٣- بنزويل – بريدين -٢- كاربوكسيلك اسيد مع فسفور اوكسي كلورايد ليعطي المركب (١)، والذي يتفاعل مع الهيدرازين ليعطي بيريدازين – ٨ – اون (٢) . و بدوره يتفاعل مع فسفور اوكسي كلورايد ليعطي المركب المعني (٣)، عند بتفاعله مع ٤- تولوين سلفونيل كلورايد اعطي المركب المطلوب كلوروبريدازين(٤).المركب (٣) يعتبر الماده الاوليه والمفتاح لتخليق جميع المركبات الاخرى، اما تفاعله مع ازيد الصوديوم اعطي مشتق التترازول (٥) . كذلك عند تفاعله مع الامنيات الاليفانية والاروماتية اعطي المشتقات (١٣،٧،٦) بينما يتفاعل المشتق (٣) مع الالانين والبيتاالانين ليعطي كل من المشتقات (١٠،٩) والتي عند حولقتها مع الاستيك انهيدريد تكون مشتقات البريميدين -٤- اون والايميدازول (١٢،١١) على الترتيب .

من جهة اخرى ،عند تفاعل المركب (٣) مع الفينل هيدرازين والثايو سيميكاربازايد اعطي الترايازولات (١٤،٨) على الترتيب وبتكاثف مجموعه الامين في الترايازول (١٤) مع كاربونيل ٢ – برموبنزا لديهايد اعطي مشتق قاعدة شيف (١٥) والذي حولق مع ازيد الصوديوم ليعطي ايميدازول (١٦) .

ان معاملة المركب (٣) مع ثايوسيانيت الامونيوم اعطي المركب (١٧) والذي يتفاعل مع الفينل ثايوسيانيت ليعطي المشتق (١٨) .المركبات المحضرة شخصت عن طريق اطياف الاشعة فوق البنفسجية ، الاشعة تحت الحمراء ، الرنين النووي المغناطيسي للهيدروجين والكاربون (١٣) .

ABSTRACT

In this study, (18) derivatives containing fused heterocyclic rings were synthesized ,in the first route 3-benzoyl-pyridin-2-carboxylic acid wasconverted to derivation (1) after reacted with phosphorus oxychloride , Cyclized (1) with hydrazine produced pyridzine-8-one (2) which reacted with 4-toluene sulphonyl chloride to afford derivative (4) . Reaction of pyridazinone (2) with phosphorus oxychloride gave the title compound chloropyridazine derivative (3). Derivative (3) was a key and starting material to synthesize all thr others compounds, that when treated with sodium azide gave tetrazole derivative (5). Also when reacted with aliphatic or aromatic amines gave derivatives (6, 7, 13). While reaction of (3) with alanine and β-alanine afforded derivatives (9, 10) which cyclized with acetic anhydride to form pyrimidine-4-one and imidazole derivatives (11, 12) respectively.

On the other hand , reaction of compound (3) with phenylhydrazide and thiosemicarbazide producedtriazole derivatives (8,14) respectively .Then, condensation of amino group of triazole (14) with carbonyl group of 2-bromo benzaldehyde formed Schiff base (15) which then cyclized with Sodium azide to produce imidazole (16).

Besides that, treatment of (3) with amoniumthiocyanat produced compound (17) which cyclized with phenyl isocyanate to form derivative (18). The synthesized structures were supported by U.V, FT-IR, ^{1}HNMR and most of them by ^{13}C-NMR spectra.

Keywords:chloropyridazine ,pyrimidine-4-one, imidazole andtetrazole derivative.

INTRODUCTION

Fused pyridine ring frameworks need accepted respectable consideration because of their different living activity[1]. Most of heterocyclic compounds containing pyridine rings are showed biological activities such as antimicrobial ,anticancer , anticonvulsant, antiviral , anti-HIV , antifungal and antimycobacterial activities[2].

Nitrogen-containing heterocyclic compounds are one of the most fruitful and extensively developing fields of heterocyclic chemistry[3].Pyridazine frameworks bring accepted significant consideration clinched alongside late decades because of their living exercises Likewise antiplatelet agents1, inhibitors of glycogen synthase kinase, antimicrobial agents3 and so forth. , Also these pharmacological exercises bring propelled chemists to integrate substituted pyridazine frameworks in place on investigate the convenience about this heterocyclic template4.

Over those a considerable length of time triazoles have turned a critical class of heterocyclic exacerbates over natural amalgamation because of their Different living properties. It will be great referred to that 1,2,4-triazole subsidiaries need restorative requisitions. . Thus there are different pills incorporating over their

structure the 1,2,4-triazole ring utilized similarly as antifungal ,antiviral agents, aromatase inhibitors. It need been accounted that structural properties for triazoles, such as moderate dipole character, hydrogen holding capability, unbending nature Furthermore soundness under in vivo states would the primary purposes behind their predominant pharmacological exercises[5]. Also, the azole derivatives, (Imidazoles andtriazoles) restrain those biosynthesis for contagious sterols, through the restraint from claiming lanosterol 14 α-demethylase, need aid regularly utilized as to start with offering medications to treat open Polaroid infections. Triazoles need likewise been joined clinched alongside An totally mixture about therapeutically fascinating drugs, including H1/H2 histamine receptor blockers, CNS stimulants, antianxiety agents, What's more sedatives[6]. Those imidazole (1,3-diaza-2,4-cyclopentadiene) is a planar, five membered heteroaromatic molecule with 3C and 2N atom in 1 and 3 positions.It might have been 1st named as gluoxaline (first synthesis with glyoxal and ammonia). Amphoteric way may be powerless to electrophilic Furthermore nucleophilic attack. Exceedingly stable to thermal, acid, base, oxidation Furthermore diminishment states. It has extensive intramolecular hydrogen bonding. It exists to two equal tautomeric structures Since the hydrogen atom might be spotted looking into Possibly of the two nitrogen atoms. The compound is ordered as aromatic because of the vicinity of a sextet for π-electrons, comprising of a match about electrons starting with the protonated nitrogen particle Also you quit offering on that one starting with each of the remaining four atoms of the ring[7]. Imidazole rings would generally utilized Likewise spin-trapping species in the fascinating provision of planning medications for neuroprotective activity[8].

A standout amongst the practically paramount requisition for imidazole subsidiaries will be their utilization Similarly as material to medication about denture stomatities. Those helter skelter restorative properties of the imidazole related medications have urged those medicinal chemists to integrate an extensive amount from claiming

novel chemotherapeutic functions. Imidazole pills have increased extent in clinical medicine[9]

Schiff base build would the intensify holding azomethine one assembly (-HC=N-). They are buildup from reaction of ketones (or) aldehydes (aldehyde and ketones) with primary amines Also were initial accounted by hugo Schiff for 1864. Framing from claiming Schiff base by takes put under acids or base catalysis alternately for high temperature. Those regular Schiff base need aid crystalline solids, which are feebly essential Anyway no less than A percentage type insoluble salts for solid acids[10].Schiff bases are the important class of ligands and have wide applications in biological, clinical, explanatory and modern investigations inaddition with their imperative parts on catalysis in organic synthesis. Some Schiff bases were tried to fungicidal movement which may be identified with their compound structure. Fragrant Schiff bases alternately their metal complexes catalyze responses for oxygenation, hydrolysis, electro-reduction What's more decomposition[11] .

Tetrazole may be a heterocyclic compound holding a carbon atom Furthermore four nitrogen atoms. An five-membered ring[12]. Tetrazole (CN4H2); its nitrogen content will be 80% of the downright weight of the molecule, the biggest rate "around stable unsubstituted heterocyclic frameworks. In spite of those secondary nitrogen content, tetrazole,the greater part from claiming its subsidiaries would generally stable, looking into warming alternately under microwave irradiation What's more likewise in the vicinity of Different compound reagents (oxidants, acids, bases, alkylating agents, dienophiles, and so on.). On regularly happening molecules, the tetrazole part will be essentially needing. Yet, its vicinity Previously, metabolic items from

claiming some protozoa might have been news person. The tetrazolyl framework will be of the same degree surprising Previously, structure What's more exceptional over acid-base aspects. To instance, compared with other thermally and synthetically stable azoles, tetrazoles have abnormally helter skelter acridity What's more exact feeble basicity13.Combined pyrimidines keep to pull in respectable consideration due to their extraordinary useful usefulness, fundamentally because of really totally range for living exercises. This is apparent particularly from publications from claiming standard reviews on the science of frameworks the place the pyrimidine ring will be combined on Different heterocycles for example, such that purines, quinazolines, pyridopyrimidines, triazolopyrimidines, pyrazolopyrimidines, pyrimidoazepines, furopyrimidines What's more pyralopyrimidines[14].

MATERIALS AND METHODS

Melting point were determined on Gallen – Kamp (MFB- 600) melting point apparatus and are uncorrected. The IR spectra of the compounds were recorded on Shimadzu FT-IR 3800 spectrometer as KBr disk .The U.V spectra were performed on Cintra-5-Gbes scientific equipment. The ^{1}H-NMR and ^{13}C-NMR spectra (solvent DMSO) were recorded on Bruker 300 MH_Z spectrophotometer using TMS as internal standard in chemistry department-AL-Byat university\ Jordan.

General procedure for the synthesis of compounds

Synthesis of compound (1)[15]

A solution of (0.01 mol., 2.36 g) of compound and(20) mL of phosphorus oxychloride might have been refluxed for 3 hrs., then poured onto 200 mL ice-sodium carbonate solution.The resulting solid was filtered, washed with water, dried and crystallized from ethanol50%.

Synthesis of compound (2)[15]

A solution of the acid chloride (1) (0.01 mol , 2.55g) Furthermore (20 mL) of hydrazine refluxed for 8 hrs and then cooled. After dilution with water, the robust precipitated might have been filtered, dried Furthermore solidified from di ethyl ether.

Synthesis of compound (3)[16]

A mixture of pyidazinnone 2 (0.01mol.,2.32 g) and PCl5 (0.01 mol) in 15 mL of POCl 3 was refluxed on a water bath for 3 hrs. Then the mixture was cooled to room temperature and poured into crushed ice slowly. The solid formed was filtered off, washed with cold water, dried Furthermore recrystallized fromtoluene to provide for 3.

Synthesis of compound (4)[17]

4-Toluenesulfonyl chloride (0.01mol., 1.58 g) was added to a mixture of derivative(2) (0.01 mol., 2.32g) and anhydrous K_2CO_3 (0.01mol.,) in dry acetone (25 mL) and the Those mixture might have been poured on100ml water the strong that differentiated around cooling might have been recystallized with benzene on provide for compound 4

Synthesis of compound (5)[18]

To a solution of compound 3 (0.01 mol.,2.51g) in absolute ethanol (50 mL), sodium azide
(0.01 mol., 0.64 g) was added and the reaction mixture was refluxed for 40 hrs. Then afterward fruition of the reaction, the response mixture might have been cooled and the precipitate that framed might have been filtered, washed with water dried and solidified from methanol should provide for the product(5).

Synthesis of compound (6)[17]

Methylamine (0.01mol) was added to a mixture of compound **3** (0.01 mol.,2.51g) in dry benzene (50 mL) and the reaction mixture was heated in oil bath for 6 hrs. The solid that separated on cooling was recrystallized from benzene to give compounds **6**.

Synthesis of compound (7)[17]

Anthranilic acid (0.01mol.,) might have been included will a mixture of 3 (0. 01 mol. , 2. 51g) refluxed in dry benzene (5 mL) and the response mixture might have been refluxed for 6 hrs.The solid that separated on cooling was recystallized from benzene to give 7 Likewise a brown solid.

Synthesis of compound (8)[16]

A solution of phenyl hydrazide (0.01 mol.,1.36g) in toloune (10 mL) was added to the solution of **3**(0.01mol.,2.51g) in 40 mL of tolouene and the mixture was heated under reflux for 8 hrs. The product that separated upon cooling was filtered, washed with benzene, and crystallized from chloroform to give derivative (8).

Synthesis of compound (9,10)[16]

(0.01 mol) of β-alanine or alanine and sodium carbonate (0.01 mol.,1.04g) were dissolved in water (25 mL), and then adjusted to pH 9-9.5. Then compound **3**(0.01 mol.,2.51g) was added to it and refluxed at the same pH for 8 hrs. The reaction mixture was left overnight at room temperature, and then treated with cold hydrochloric acid (pH 0.5). The solid product obtained was filtered off, washed with water, and recrystallized from an appropriatesolvent to give the target compounds.

Synthesis of compound (11,12)[16]

A mixture of derivatives(0.01 mol), acetic anhydride (30 mL), and anhydrous sodium acetate (0.01mol. ,0.82 g) was heated under reflux for 3 hrs. Then,the mixture was cooled, filtered,washed with water, dried, and crystallized from appropriate solvent to give 11,12.

Synthesis of compound (13)[16]

A mixture of compound 3 (0.01 mol., 2.51g) and *o*-phenylenediamine (0.01 mol., 1.04 g,) was heated in a fusion tube provided with an air condenser in an oil bath at 170-180 ◦C for 2 hrs. After cooling (to room temperature), the reaction mixture was poured into cold water (100 mL). Then the manufacturing was recrystallized frompetroleum ether (60-80) to give 13.

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Synthesis of compound (14)[16]

A mixture of compound 3 (0.01 mol., 2.51g) and thiosemicarbazide (0.01 mol) in absolute ethanol was refluxed for 8 hrs. The solid product obtained upon cooling was filtered off, dried, and crystallized from fit solvent.

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Synthesis of compound (15)[19]

(0.01 mol.,) of O-bromo benzaldehyde was mixed with equivalent amount of corresponding derivative (14) in 30 mL of ethanol. The resulting mixture was left under reflux for 2 hrs and the solid product formed was separated by filtration, washed with water, and then dried, purified by recrystallization from ethanol.

Synthesis of compound (16)[20]

A mixture of imine derivative (15) (0.01 mol) and sodium azide (0.01mol., 0.64g) in (25 mL) of dry dioxan , was refluxed on a water bath for 5hrs, The reaction mixture was allowed to cool down to room temperature , filtered and recrystallized from ethanol , this reaction monitoredby T.L.C. (benzene:ethanol)(1:1) .

Synthesis of compound (17,18)[16]

The solution of ammoniumthiocyanate (0.01 mol) in dry acetone(20 mL) was added to a stirred solution of compound 3(0.01 mol., 2.51g) in dry acetone(30 ml). The reaction mixture was stirred for 1 h at room temperature. Ammonium chloride was precipitated during the progress of the reaction. After filtration of the ammonium chloride, phenyl isocyanate (0.01 mol., 1.2 g) was added to the filtrate. The reaction mixture was heated under reflux for 30 min. The solid product that separated after cooling was crystallized from ethanol to give derivative (18) .

Results and Discussion

The starting material (3-benzoyl-pyridine-2-carbonyl chloride) (1) was synthesized by reaction of (3-benzoyl-pyridine-2-carboxylic acid) with phosphorus oxychloride. compound (1) was characterized by U.V spectrum which showed two absorption bands at wave length (230, 291) nm due to $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ respectively .FT-IR spectrum gave stretching vibration at 1695 cm^{-1} due to carbonyl of ketone and another at 1785 cm^{-1} due to COCl , another band at 840 cm^{-1} due to C-Cl . ^{1}H-NMR gave a signals which Listed in table (2).

Cyclization of compound (1) with hydrazine gave derivative (2) , The pyridazine-8-one was showed a band at 3220cm^{-1} due tostretching vibration of NH , and 1660cm^{-1} attributed to carbonyl of ring . U.V and ^{1}H-NMR date are listed in table (2).

The target 8-chloro-5-phenyl-pyrido[2,3-d] pyridazine (3) was synthesized by reaction of (2) with phosphorus oxychloride , No evidences for the presence of stretching vibration of carbonyl group was seen in FT-IR spectrum 0f (3) , while showed a band at 845 cm^{-1} due to stretching vibration of C-Cl .

^{1}H-NMR of derivatives (3) gave the following signal in ppm : (7-7.4) for protons of phenyl ring . (7.5-8.6) for protons of pyridine ring . Also ^{13}C-NMR spectra of (3) agree with their assigned structure. The reaction of derivative (2) with 4-toluene sulfonyl chloride and K_2CO_3 in dry acetone gave derivative (4). The last gave absorption bands at (248 , 297) nm due to $\pi\rightarrow\pi^*$ & $n\rightarrow\pi^*$ respectively . FT-IR spectrum was showed a band at 1335 cm^{-1} due to SO_2 and another at 1640 due to C=N , 1672 attributed to carbonyl of pyridazinone ring two bands at (2920 , 2860) cm^{-1} due to CH alph . ^{1}H-NMR and ^{13}C-NMR gave a signals are listed in table (2). Compound (3) used as starting material for synthesized many fused rings, for

example, Compound (5) was furnished via treatment of derivative (3) with sodium azide in ethanol as shown in scheme (2). Derivative (5) was found to be in tautomeric equilibrium with azido derivative (5'), Its FT-IR spectrum revealed the absence of band at 845 cm^{-1} which due to C-Cl and showed new band at 2150 for N_3 and another at 1615 cm^{-1} due to C=N . The ^{1}H-NMR and ^{13}C-NMR spectra gave signals data listed in table (2).

In addition for above , derivative (3) reacted with methyl amine and produced derivative (6) , whose structure was inferred from its FT-IR , ^{1}H-NMR and ^{13}C-NMR spectra . FT-IR spectrum showed a band at 3380 cm^{-1} due to NH group, (2927, 2880) cm^{-1} due to stretching vibration of CH alph .^{1}H-NMR gave the following data in ppm : 2.5(S,3H,CH_3) , 4(S,1H,NH) , (7-7.4)aromatic protons of phenyl ring , (7.5-8.6) aromatic protons of pyridine ring . While ^{13}C-NMR data listed in table (2).

In addition , reaction of (3) with anthranilic acid to give compound (7) , this derivative confirmed by FT-IRspectrum which showed a band at 1670 cm^{-1} due tocarbonyl of ring and at 1641 $cm^{-1}$for C=N and anotherbands are listed in table (2) .Also , spectral data of ^{1}H-NMR and ^{13}C-NMR for compound (7) listed in table (2) . on the other hand , the reaction of (3) with benzoic acid hydrazide afforded triazolederivative (8) which characterized by U.V , FT-IR , ^{1}H-NMR and ^{13}C-NMR spectra . The data of spectra are listed in table (2) .

Its worth to mention, Reaction ofderivative(3) with alanine and β-alanine under reflux conditions produced the corresponding derivatives (9, 10) respectively. FT-IR spectra gave new bands at (1710 , 1715) cm^{-1} forcarbony of carboxylic acid and revealed a board absorption band at (3200-3400) , (3190-3395) cm^{-1} attributable

to OH group and (3450 , 3435) cm^{-1}due to stretching vibration for NH group ofderivatives (9 , 10) respectively . The amino acid derivatives (9, 10) were easily cyclized in acetic anhydride in the presence of anhydrous sodium acetate to yield derivatives (11 , 12) , Their spectral data are listed in table (2) . Reaction of derivative (3) with aromatic amine (phenylene diamine) afforded derivative (13) which confirmed by FT-IR.The FT-IR spectrum showed a band at 1640 cm^{-1} due to C=N of imidazole ring and another at 3080 cm^{-1} for CH arm. , while ^{1}H-NMR gave the following signals in ppm : (7-7.5) foraromatic protons of phenyl rings , (7.7-8.6) for aromatic protons of pyridine rings. Besides that , ^{13}C-NMR gave the following data : 127 , 129 , 135 , 149 , 141 , 137 , 115 , 122 , 159 , 161.

Treatment of (3) with thiosemicarbazide produced amino thiazolderivatives (14) which when allowed for condensation with o-bromo benzaldehyde to afford azomethin derivative (15). Derivatives (14) confirmed by U.V,FT-IR and^{1}H-NMRspectra.U.V spectrum showed two band at (258, 323) nm due to $\pi\rightarrow\pi^{*}$and $n\rightarrow\pi^{*}$transition respectively.FT-IR spectra of (14) showed new bands at (3400, 3480) cm^{-1}due to NH_2, also ^{1}H-NMRspectrum showed a singlet signal at 4.5 ppm due to proton of NH_2 and another signal arelisted in table (2) .

In FT-IRspectrum of (15) showed disappearance of band of NH_2 and showed new band at 1625 cm^{-1} due to stretching vibration of azomethine group (C=N) , similarly, ^{1}H-NMR spectrum gave a signal at 8.2 ppm due to (-N=CH) and another as observed in table (2) . Tetrazolederivative (16) was synthesized by reaction of Schiff base (15) with sodium azide . ItsFT-IRspectrum showed disappearance of absorption band at 1683$cm^{-1}$of (C=N) anddisappearanceof absorption band at 1683

cm^{-1} due to(C=N) of tetrazole ring ,while showed a band at $1430cm^{-1}$ due to(N=N) . Spectral data for $^{1}H-NMR$ and $^{13}C-NMR$ spectral are listed in table (2) .

Furthermore, the reaction ofderivative (3) with ammonium thiocyante afforded the intermediate (17) that reacted with phenyl isocyanate via cycloaddition reaction to yield derivative (18).

The FT-IRspectrum ofderivative (18) revealed the presence of CO group of ring at 1678 cm^{-1} and showed presence absorption band at $1265cm^{-1}$ due to (C=S) , $1630cm^{-1}$ for (C=N) . Spectral data for $^{1}H-NMR$ and $^{13}C-NMR$ are listed in table (2)

Table (1): physical properties of synthesized compounds

Comp. NO.	M.p. ^{0}C	Yield %	Color	Recryst. Solvent
1	117-119	91	Yellow	Ethanol 50%
2	125-127	87	Brown	di ethyl ether
3	204-206	90	Dark yellow	Toluene
4	131-133	80	White	Benzene
5	157-159	71	White	Methanol
6	99-101	65	Light brown	Benzene
7	166-	78	Brown	Benzene

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8	183-185	67	Off-white	Chloroform
9	141-143	59	Pale yellow	Ethanol 50%
10	152-154	63	Yellow	Ethanol 50%
11	175-177	89	Orange	Chloroform
12	160-162	73	Dark yellow	Chloroform
13	213-215	62	Grey	Petroleum ether (60-80)
14	189-191	85	Brown	Ethanol
15	220-222	93	Dark red	Ethanol
16	243-245	70	Orange	Ethanol
18	256-458	75	White	Ethanol

Table (2): Spectral data of synthesized compounds

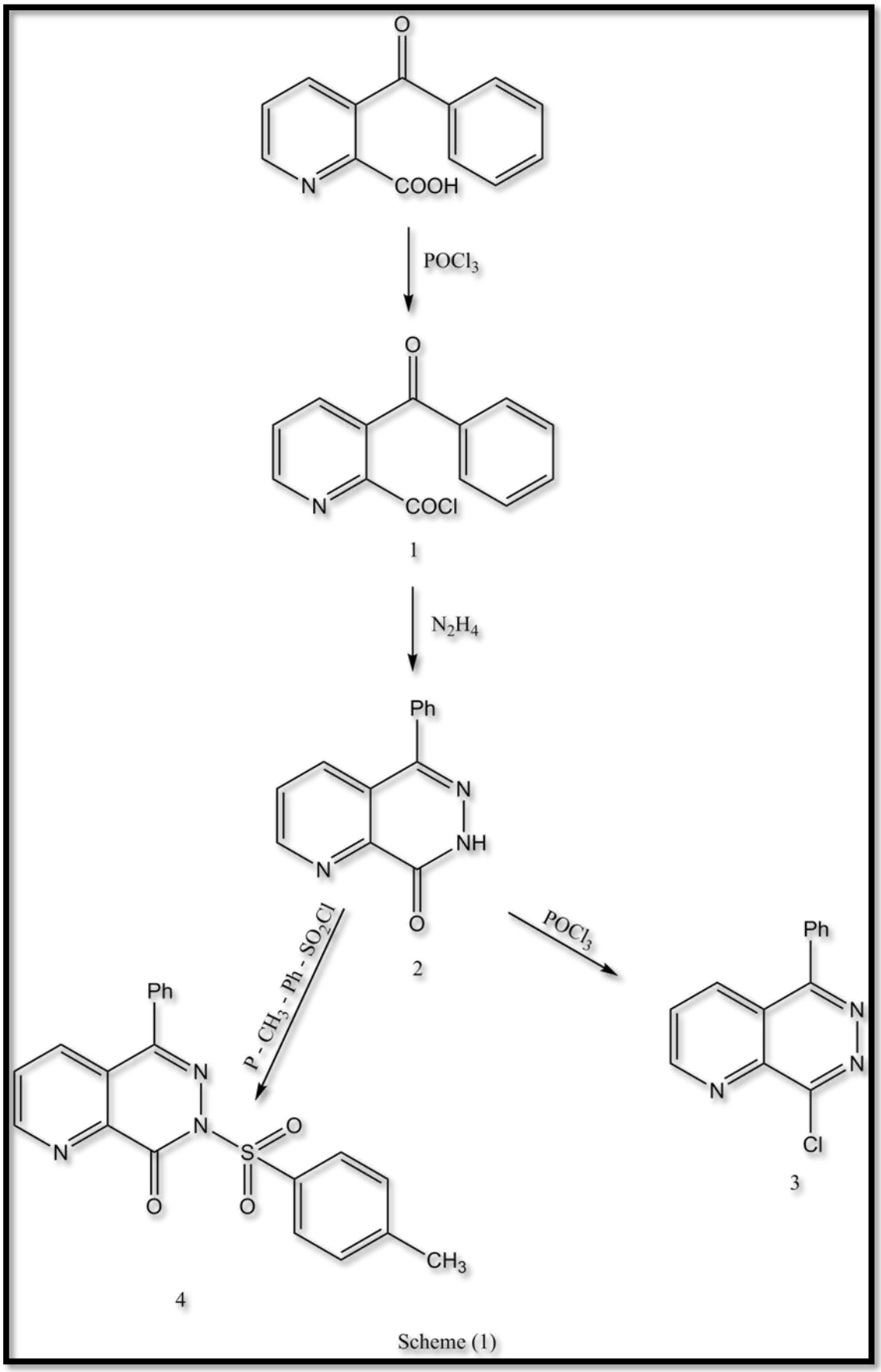
Comp. NO.	U.V λ_{max} nm	FT-IR	^{1}H-NMR	^{13}C-NMR
1	230 291	1695 for CO Ph 1789 for COCl 3085 for CH arom. 1550 for (C=C) arom. 840 for C-Cl	(7.4-7.8) for arom. Protons of Ph. Ring. (8.2-9.4) forarom. Protons of pyridine ring.	128,132,129, 133,138,169, 127 154,163,187
2	242 287	3220 for NH 1660 for CO of ring , 3091 for CH arom. 1590 for C=N	6.8 (S,1H,NH) (7.4-7.8)forarom. Protons of Ph. Ring. (8-9.2) for arom. Protons of pyridine ring .	
3	255 274	3100 for CH arom. 1610 for C=N 845 for C-Cl	(7-7.4) for arom. protones of Ph ring . (7.5-8.6) for arom. Protons of pyridine ring .	128,129,127, 123 135,149,137, 150 157
4	248 297	1335 for (SO_2). 1615 for C=C. 1640 for C=N. 1672 for CO of	2.4 (S,3H,CH_3) (7-7.8) for arom. Protons. ofPh ring . (8-9.1) for arom.	21,128,130,1 32, 137,125,129, 136,140,150,

		pyrizinone ring. 2920, 2860 for CH arom.	Protons of pyridine ring.	152,21,170
5	237 300	1615 for C=N of tetrazole ring. 3079 for CH arom. 1597 for C=C. 2150 for N_3.	(7-7.4) for arom. protons of Ph ring . (7.6-8.5) for arom. protons of pyridine ring .	123,127,129, 125 136,138,148, 159
6	229 273	3380 for NH . 2927 , 2880 for C=N 1605 for C=N	2.5 (S,3H,CH_3) 4 (S,1H,NH) (7-7.4) for arom. Protons of Phring . (7.5-8.6) arom. Protons of pyridine ring.	35,123,127,129, 135,113,149, 159,150
7	250 281	3083 for CH arom. 1609 for C=C . 1641 for C=N . 1670 for CO of ring	(7-7.4) for arom. protons of Ph ring . (7.7-8.9) arom. Protons of pyridine ring.	128.129,131, 122, 151,156,155, 136 131,133,164
8	248 279	1630 for C=N of tri azole ring . 1620 for C=C .	(7-7.4) for arom. protons of Ph ring . (7.5-8.6) arom.	127,129,123, 125 136,148,136,

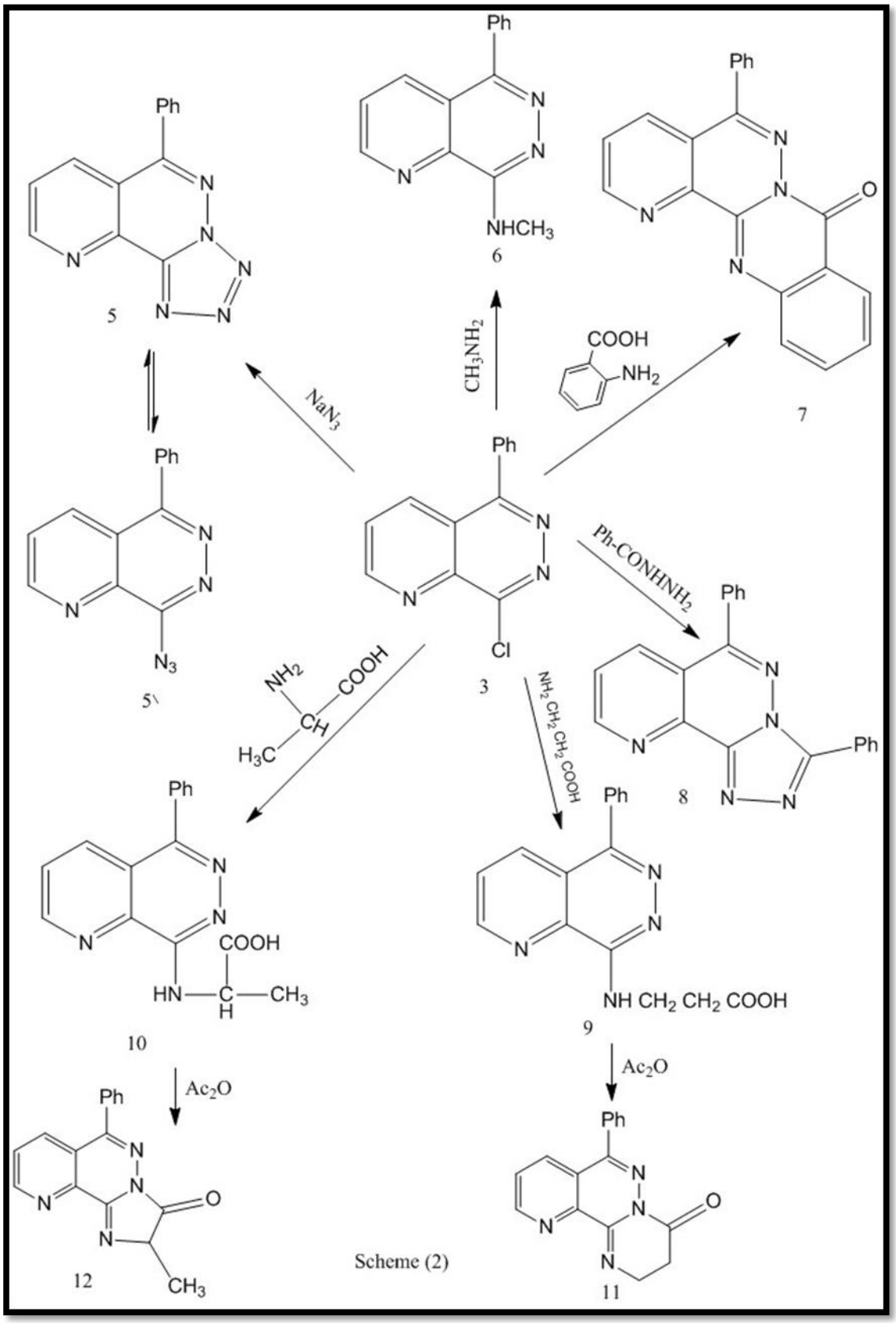
		3075 for CH arom.	Protons of pyridine ring.	150
9	232 270	1710 for CO of carboxylic acid . 3200-3400 broad for OH of carboxylic acid . 3450 for NH . 2926 , 2871 for CH alph.	4.2 (S,1H,NH) 3.4 (T,2H,NH-$\underline{CH_2}$) 2.5 (T,2H,NHCH$_2\underline{CH_2}$) 11(S,1H,OH) of carboxylic acid (7-7.4) for CH arom. protons of Ph ring . (7.5-8.6) arom. Protons of pyridine ring .	
10	225 267	1715 for carboxylic acid . 3190-3395 of OH of carboxylic acid . 3435 for NH . 2990 , 2880 for CH alph.	4 (S,1H,NH) 1.3 (d,3H, CH-$\underline{CH_3}$) 3.7 (q,2H,NH-$\underline{CH}$-CH_3) 11(S,1H,OH) of carboxylic acid.	16,62,177,159,113, 159,149,123, 127, 135,148,13,128,129
11	251 312	1675 for CO of ring . 1613 for C=N . 3092 for CH	1.5(T,2H,$CH_2$of pyrimidine-4-one) . 2.5(T,2H,CH_2COof pyrimidine-4-one) .	

		arom.	(7.2-7.6) for arom. protons of Ph ring . (7.8-9.1) arom. Protons of pyridine ring	
12	238 307	1687 for CO of ring . 1610 for C=N. 1597 for C=C. 2945 , 2883 for CH alpha	2.7(q, 1H, CH of ring) 1.2(d, 3H, CH_3subst. on ring) (7-7.4) for arom. protons of Ph ring . (7.8-9.1) arom. Protons of pyridine ring.	
13	255 310	1640 for C=N of ring 1625 for C=C . 3080 for CH arom.	(7-7.5) for arom. protons of Ph ring . (7.7-8.6) arom. Protons of pyridine ring .	127,129,135, 149, 141,137,115, 122, 159,161
14	258 323	3400 , 3480 for NH_2 . 3075 for CH	4.5 (S,1H,NH_2). (7.2-7.4) for arom. protons of Ph ring .	

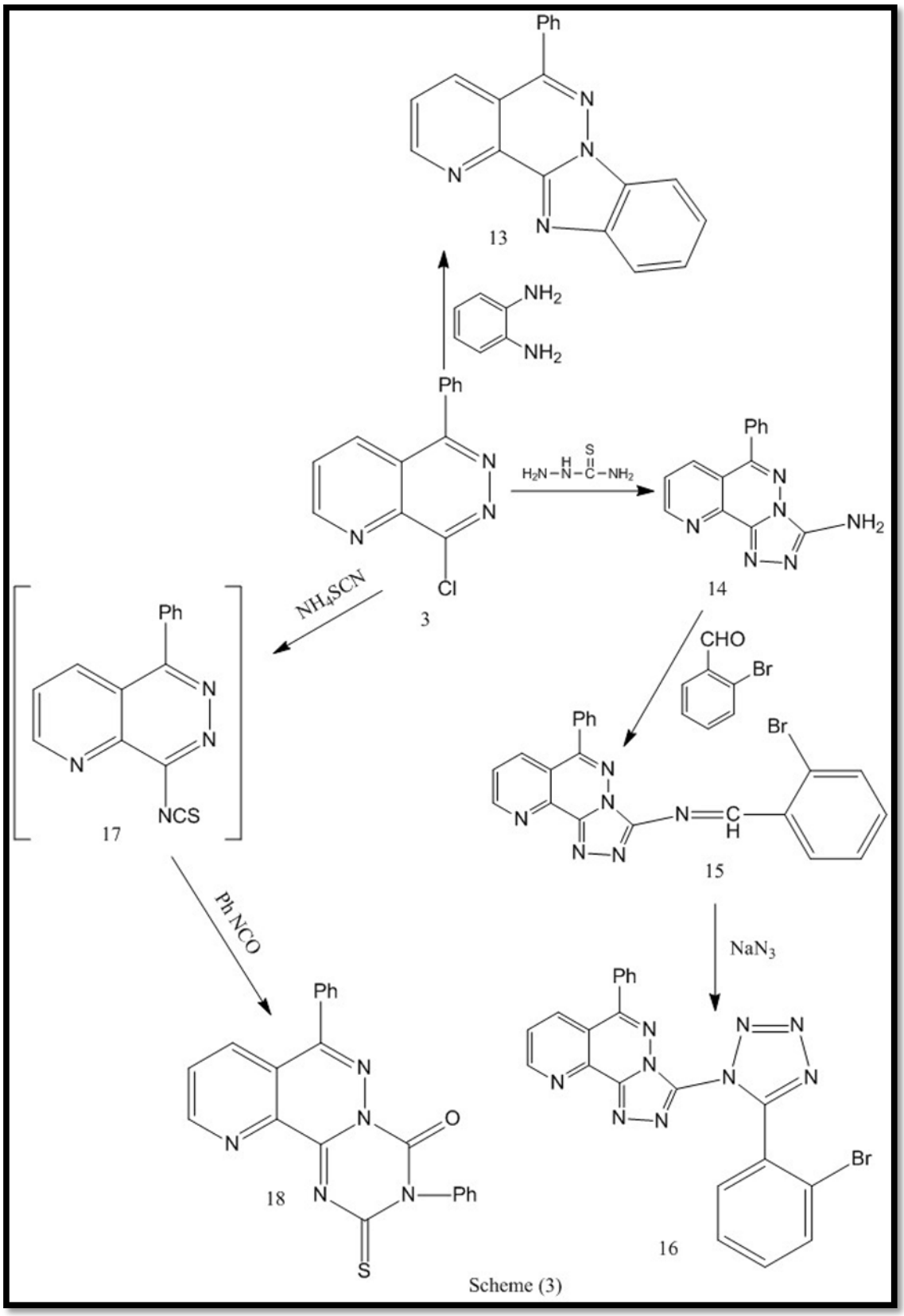
		arom. 1637 for C=N .	(7.5-8.6) arom. Protons of pyridine ring.	
15	267 331	1625 for C=N of azo methin group 750 for C-Br 3095 for CH arom.	8.2 (S,1H,CH=N). (7-7.5) for arom. protons of Ph ring . (7.4-8.6) arom. Protons of pyridine ring .	127,129,135, 123, 149,136,159, 148, 163,133,131
16	249 327	743 for C-Br. 1683 of C=N of tetrazolering . 3087 for CH arom. 1597 for C=C. 1430 for N=N.	(7-7.4) for arom. protons of Ph ring . (7.5-8.9) arom. Protons of pyridine ring .	127,129,125, 123, 146,148,139, 132, 130,159,135, 121
18	245 320	1678$cm^{-1}$for CO group of ring. 1265cm^{-1} for (C=S) , 1630$cm^{-1}$for (C=N)	(7-7.5) for arom. protons of Ph rings . (7.8-9.1) for arom. Protons of pyridine ring .	123,128,130, 131,136,120, 125,152,154, 157,164,180


O
N
COOH
POCl3
O
N
COCl
1
N2H4
Ph
N
NH
N
O
2
POCl3
P - CH3 - Ph - SO2Cl
Ph
N
N
N
O
S
O
O
CH3
4
Ph
N
N
N
Cl
3

Scheme (1)


Ph
N
NHCH3
6
CH3NH2
NaN3
5
5'
N3
3
Cl
COOH
NH2
7
O
Ph-CONHNH2
8
Ph
NH2
COOH
CH
H3C
NH2 CH2 CH2 COOH
9
NH CH2 CH2 COOH
10
HN
C
CH3
Ac2O
12
11

Scheme (2)


Ph
N
N
N
13
NH2
NH2
Ph
N
N
N
Cl
3
H2N–N–C–NH2
S
H
Ph
N
N
N
N
NH2
14
NH4SCN
CHO
Br
Ph
N
N
N
NCS
17
Br
N=C
H
N
N
N
15
PhNCO
NaN3
Ph
N
N
N
O
N
N
Ph
S
18
Ph
N
N
N
N
N
N
N
Br
16

Scheme (3)

References

1- H. Al-Kashef ; AR. Farghaly ; A. Al-Hazmi ; Th. Terme and P. Vanelle. J, mol .15 , 2651-2666 . 2010 ."pyridine Based Heterocycles . Synthesis of new Pyrido [4′ , 3′ , 4 , 3] thieno [2,3-d] pyrimidines and Related Hetero cyclic " .

2- S. Abdul Rahman. J. mole. 17 , 10902-10915 , 2012 . " Synthesis of new series of Pyridine and Fused Pyridine derivatives " .

3- I. Othman ; H. Nasr and M. Hassan , Research Article . Canadian Chemical Transactions .2 . 504-517 .2014 ."Synthesis of Some Novel Pyridazine, Thienopyridazine, Pyrazolopyridine, Pyridopyrazolopyrimidine and Pyridopyrazolotriazine Derivatives with Their Antimicrobial Activity.

4- D.Ünal ; E. Saripinar and Y. Akcamur. Turk. J. Chem. 30, 691-701, 2006. "A New Method for the Preparation of PyridazineSystem : Experimental Data and Semiempirical PM_3 Calculations " .

5- S. Felicia ; D. Carolina ; G. Saramet ; V. Uivarosi ; C. Draghici and V. Radulescu . Int. J. Mol. Sci. 15 , 10908-10925 . 2014 ." Synthesis and Antiovidant Activity Evaluation of New Compounds from Hydrazine-Carbothioamide and 1,2,4-Triazole class containing Diarylsulfone and 2,4-Diflurophenyl Moieties " .

6- H. Dalloul. Research Article . Canadian Chemical Transaction . 3,108-117 , 2015 . " Synthesis of new 1,2,4-Triazole Derivative via 1,3-Dipolar Cycloaddition Reaction of Nitrilimines with Hydrazones "

7- D. Romero ; V. Heredia ; O. Barradas , Ma. Lopez and E. Pavon .J ,Chem and Biochem . 2(2) , 45-83 , 2014 . " Synthesis of Imidazole Derivatives and their Biological activities " .

8- CH. Liu ; C. Shi ; F. Mao ; Y. Xu ; B. Wei ; J. Zhu ; M. xiang and G. Li , J , Mol, 19 , 15653-15672 , 2014 . " Discovery of New Imidazole Derivatives containing tho 2,4-Dienone Motif with Broad-spectrum Antifungal and Antibacterial Activity " .

9- P. Gupta and J.Gupta .Chem .Sci , J. 6 , 2015. " Synthesis of Bioactive Imidazoles " .

10- Dr.Xavier and N. Srividhya . IOSR Journal of Applied chemistry (IOSR-JAC) .7 , 6-15 , 2014 . " Synthesis of study of Schiff base Ligands " .

11- R. Radfar and A. Abedi , J . Appl .chem .Res . 9(2) , 59-65 , 2015 . " Synthesis and Characterization of New Schiff Bases of Ethylenediamine and Benzaldehyde Derivatives , Along with Their Iron Complexes .

12- CH. Wei; M. Bian and G. Gong. J, Mol. 20, 5528-5553, 2015. "Tetrazolium Compounds: Synthesis and Applications in medicine ".

13- L. Miguel ; A. Ismael and M. Lurdes . J. Mol. 15. 3757-3774. 2010. "Photochemical Transformations of TetrazoleDerivatives: Applications in Organic Synthesis ".

14- B. Musa , A. Bayoumi , M. Korraa , M. Assy and S. El-Kalyoubi . int, J. org. chem. 5 , 37-47 , 2015 . "A Novel One – Pot and Efficient procedure for Synthesis of Fused Uracil Derivatives for DNA Binding ".

15- F. Yassin . J. Micr. Antimicr. 2(7).93-97.2011. "Novel Pyrazole Pyridazine Derivatives likely to posses Anti-inflamatory Activity".

16- M. Abdel Aziz ; A. Youssef and I . Essam. Turk, J. Chem. 36, 347-366.2012. "Synthesis and antimicrobial evaluation of some annelatedphthalazine derivatives and aCyclo C-nucleosides from 1-chloro-4-(2,4,6-trimethylephenyl) phthalazine precursor " .

17- S. Abubshait . J. Mol. 12(1), 25-42, 2007. "An Efficient Synthesis and Reactions of Novel Indolyl-pyridazinoneDerivatives with Expected Biological Activities .

18- A. Al-Marhabi ; H. Abbas and Y. Ammar . J. Mol. 20, 19805-19822, 2015. "Synthesis, Characterization and Biological Evaluation of Some Quinoxaline Derivatives: A promising and Potent New Class of Antitumor and Antimicrobial Agents ".

19- M. Aqeel ; K. Mahmood and A. Wajid , International Conference on Chemistry and Chemical process . 10, 2011. "Synthesis, Characterization and Biological Activity of Schiff Bases ".

20- R. Tama . J. Karbala University , 9(3) , 2011 . " Synthesis and Characterization of Some New Tetrazole and 1,3-oxazepine Derivatives " .