Synthesis of new N-Substituted -3- chloro -2- azetidinones for 2, 4-Diamino-6-phenyl-1,3,5-triazine

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Abstract:

The current study involved synthesis of several new N-Substituted -3- chloro -2- azetidinones for 2,4-Diamino-6-phenyl-1,3,5-triazine by two steps. The first step includes preparation of Schiff bases (A1-A6) by condensation of 2,4-Diamino-6-phenyl-1,3,5-triazine with many substituted aldehydes, then the second step includes preparation new six azetidinone compounds (B1-B6) by reaction of chloro acetyl chloride with the prepared Schiff bases in first step. The prepared compounds were characterized by physical properties, FT-IR, UV and some of them by ^{1}H-NMR, ^{13}C-NMR spectroscopy were recorded.

Keywords: 2, 4-Diamino-6-phenyl-1, 3, 5-triazine, Schiffbase, azetidinones.

Introduction:

Schiff bases are characterized by the (N=CH) imines group which important compounds in medicinal and pharmaceutical field [1]. They show biological activities including antibacterial, antifungal [2,3] , anticancer [4] and herbicidal activities [5] figure (1) shows the stricture for this component. Fur their more Schiff bases have been widely used as protective group of amino group in organic synthesis [6, 7]. Schiff bases react with chloroacetyl chloride to give (β – Lactam) 3-chloro-2-azetidinones.

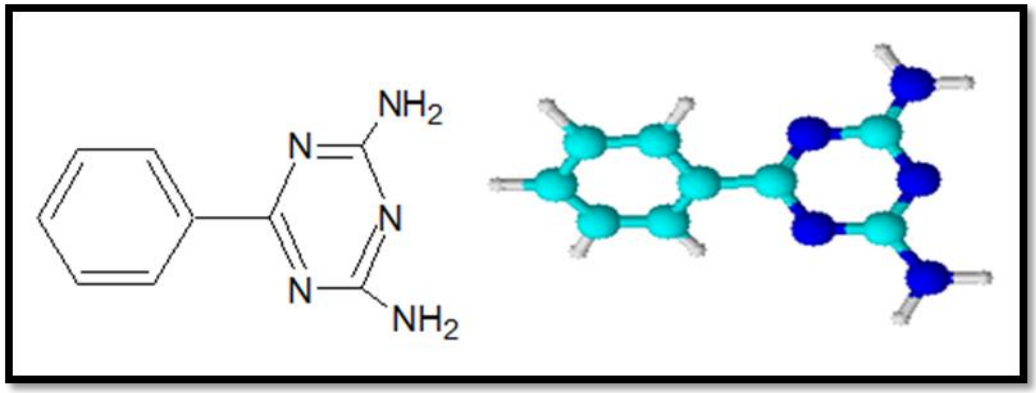

Fig.1: 2,4-diamino-6-phenyl-1,3,5-triazine

The β – Lactam hetro cycles are still the most prescribed antibiotics used in medicine. They are considered as an important contribution of science to humanity [8]. The most widely used antibiotics such as the Penicillins, Cephosporins, Carumonam, aztreonam and Nocardincins all contain β – Lactam rings [9] . The long term use of β – Lactam antibiotics exerts selective pressure on bacteria and permits the proliferation of resistant organisms [10]. A comparative study of current antibiotics with those from decades shows an alarming increase in bacterial resistance to β – Lactam antibiotics [11] .The development of several synthetic and semi-synthetic β – Lactam antibiotic by the pharmaceutical industry was due to the growing resistance of bacteria towards the β – Lactam antibiotics and the need for medicines with a more specific antibacterial activity. An interesting group of β – Lactam are the monocyclic β – Lactams, which are molecules that do not contain another ring fused to the β – Lactam one. Azetidinones, which are part of the antibiotic structure , are known to exhibit interesting biological activities [12]. Alarge number of 3-chloro mono cyclic β – Lactams possess powerful antibacterial, antimicrobial, anti-inflammatory, anticonvulsant and ant tubercular activity [13].

Material and Methods:

General:

Chemicals employed were of analytical grade and used without further purification. Melting points were determined on Gallen kamp capillary melting point apparatus and were uncorrected. FT-IR spectra were recorded using KBr discs on SHIMADZU FT-IR 8400 Fourier Trans form Infrared spectrophotomet. U.V. spectra recorded using SHIMADZU UV-visible recording spectrophotometer U.V 160. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Brukerspecrosp in Ultra shield 300 MHZ in strumentusing tetramethylsilane (TMS) as an internal standard and DMSO-d6 as a solvent in Al-Albate University in Jordan.

Preparation of Schiff base (A1-A6)

A series of Schiff bases (A1-A6) were prepared from the reaction of 2, 4-diamino-6-phenyl-1,3,5- triazine (0.01mol) with different aldehyde (0.02mol) in 25 ml ethanol absolute and drops of glacial acetic acid. This mixture was refluxed for 5hrs. The precipitate was filtered and recrystallized from ethanol and water. Melting points, yield% data are listed in table (1).

Preparation of Azetidinone from Schiff base (B1-B6) [1, 2].

To a mixture of compounds (A1-A6) respectively (0.01 mol) in N,N' Dimethyl formamide (15ml), triethylamine (0.025 mol), was added chloroacetylchloride(0.025 mol) drop-wise at 5-10 Cº.The reaction mixture

was then stirred for 6 hrs. And left at room temperature for 24 hours then poured into crushed ice. The solid separated was dried and recrystallized from ethanol and water. Melting points, yield% data are listed in Table (2).

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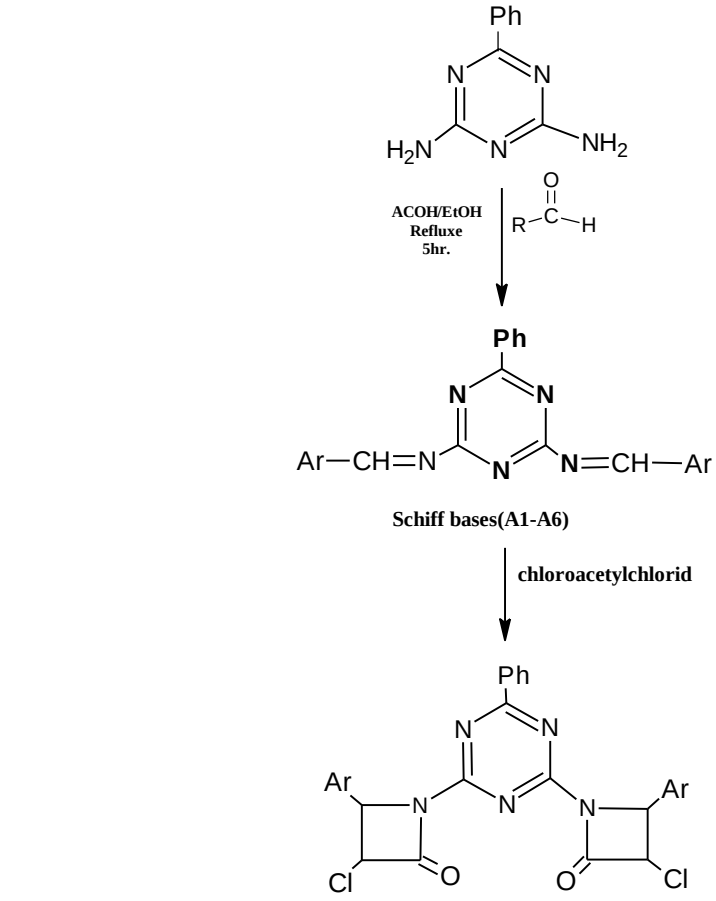
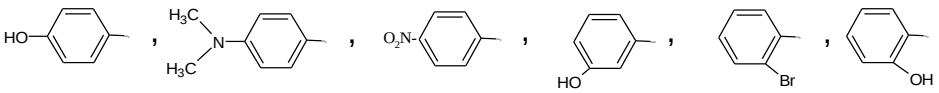


(B1-B6)

Ar = 

(Scheme 1)

Table (1) Physical Properties of Synthesized Schiff Bases (A1-A6)

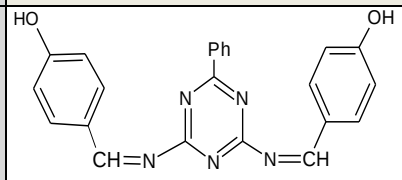
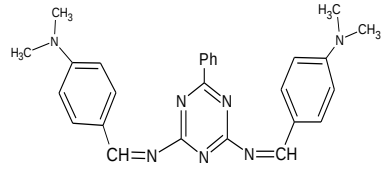
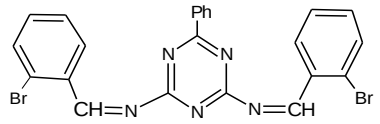
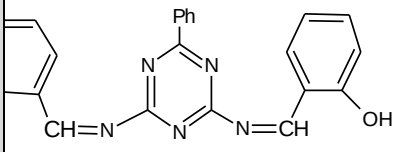
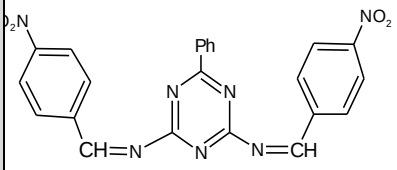
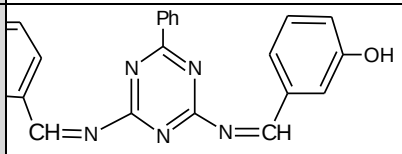
Comp. No.	Compound structure	Melting Point C°	Color	Yield %	Molecular formula	FW
A1		140-142	Yellow	63.72	$C_{23}H_{17}N_5O_2$	394.42
A2		132-134	Faint Yellow	43.63	$C_{27}H_{27}N_7$	449.55
A3		240-243	Yellow	56.58	$C_{23}H_{15}Br_2N_5$	521.201
A4		164-166	Brown	65	$C_{23}H_{17}N_5O_2$	395.41
A5		200-202	Orange	43.2	$C_{23}H_{15}N_7O_4$	453.41
A6		160-162	Dark Orange	66	$C_{23}H_{17}N_5O_2$	395.41

Table (2) Physical Properties Data of Synthesized Azetidinone Compounds (B1-B6)

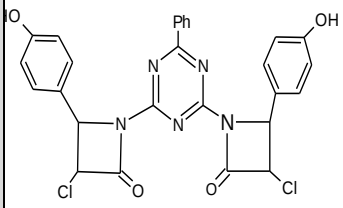
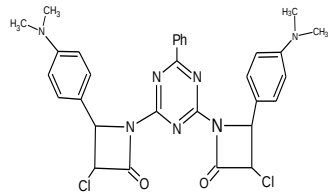
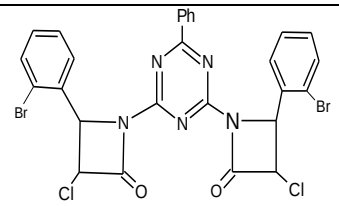
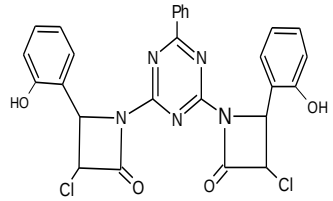
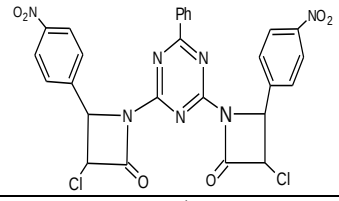
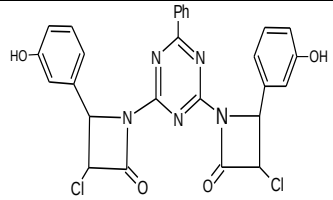
Comp. No.	Compound structure	Melting Point C°	Color	Yield %	Molecular formula	FW
B1.		129-132	Faint Yellow	59	$C_{27}H_{19}Cl_2N_5O_4$	548.37
B2		175-177	Yellow	66	$C_{31}H_{29}Cl_2N_7O_2$	602.51
B3		138-140	Orange	68	$C_{27}H_{17}Br_2Cl_2N_5O_2$	674.17
B4		100-102	Brown	57.5	$C_{27}H_{19}Cl_2N_5O_4$	548.37
B5		123-125	Brown	65	$C_{27}H_{17}Cl_2N_7O_6$	606.37
B6		237-239	Deep brown	70	$C_{27}H_{19}Cl_2N_5O_4$	548.37

Table (3) FT-IR Spectral Data for Some Functional Group for all Product Compounds

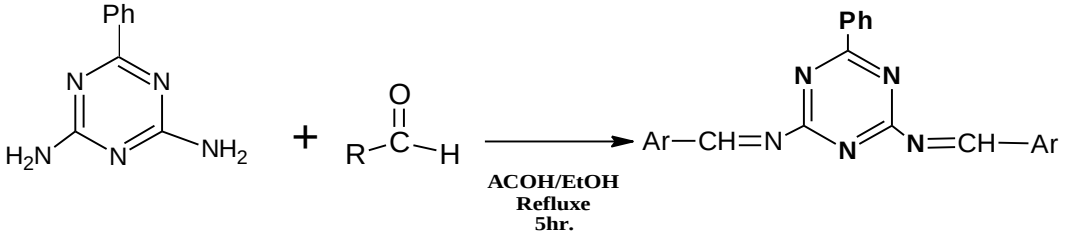
Comp. No	υ (C-H)aliphatic cm^{-1}	υ (C-H) aromatic cm^{-1}	υ (C=C) cm^{-1}	υ (C-OH) cm^{-1}	υ (C=O) cm^{-1}	υ (C-Cl)cm^{-1}	υ (C=N) cm^{-1}	Others cm^{-1}
A1.	2875	3169	1541	3305	_	1159,827	1670	_
A2.	2829-2916	3132	1535	_	_	1066,810	1662	_
A3.	2921	3219	1490-1531	_	_	_	1670	υ(C-Br) 570, 665
A4.	2850	3178	1539	3477	_	_	1624	
A5.	2850-2943	3105	1604	_	_	879 1093	1662	C-υ(NO2) 1531, 1346
A6.	2835	3070	1581-1492	3213	–	_	1670	–
B1.	2777-2989	3150	1581	3383	1735	1022, 840	_	_
B2	2881-2974	3005	1473-1597	_	1732	1037, 894	_	–
B3	2881-2978	3200	1473-1539	_	1705	1033, 875	_	υ(C-Br) 594, 690
B4	2939	3174	1620-1543	3383	1651	1072, 848	_	
B5.	2738-2974	3132	1604-1573	_	1705	1172, 852	_	υ (C-NO2) 1365 - 1396
B6	2738-2974	3190	1620-1543	3383	1689	1137,848	_	–

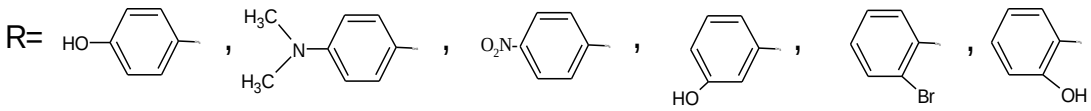
Result and Discussion:

The present work involved two steps:

First step: includes preparation of new six Schiff bases (A1-A6) were prepared from the reaction of 2, 4-diamino-6-phenyl-1,3,5- triazine with different substituted aldehyde .The synthesis of these compound was carried out lined in scheme (1), and the physical properties of Schiff bases (A1-A6) including melting point range of (132-243)ºC and % yield were range of (43.2-63.72) and these compounds were identified by FT-IR spectroscopy , FT-IR spectrum of (A1) showed characteristic absorption bands (1670)cm^{-1} , (3169) cm^{-1}, (2875) cm^{-1} and (3305) cm^{-1} due to υ (C=N) , υ(C=H) aromatic , υ (C=H) aliphatic and υ (O=H) respectively as shown in table (3) fig.(2) and FT-IR spectrum of (A5) showed characteristic absorption bands (1662)cm^{-1} , (3105) cm^{-1}, (2850-2943) cm^{-1} and (1531,1346) cm^{-1} due to υ (C=N) , υ(C=H) aromatic , υ (C=H) aliphatic and υ (C-NO_2) respectively as shown in table (3) fig.(4)

The reaction was followed by disappearance of (NH_2) absorption band at (3410-3298) $cm^{-1}$and appearance of (C=N) absorption band in the IR spectra of the products.

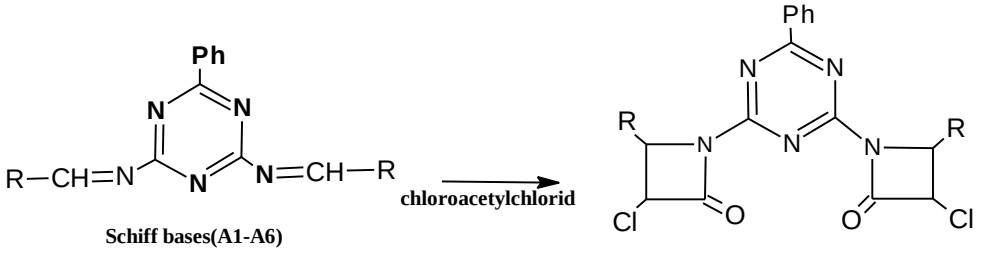


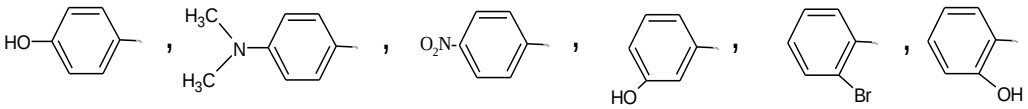


Attributed UV.spectrum of compounds (A2) and (A5) showed on absorption λ max at (335) nm and (278) nm which to ($\pi - \pi^*$) the absorption show in fig.(7),fig.(8) and fig.(6) show the U.V. spectrum for the original compound. In the ^{1}H-NMR spectrum data of compound (A5) showed signals at (8.15-8.39) ppm was attributed to proton in (N=CH), and multiples signals at (7.13-7.39) ppm due to aromatic proton, and signals at (6.74) ppm due to (O-H) proton as shown in fig (11).

In the^{13}C-NMR spectrum of compounds (A5) showed signal at (192) ppm for carbonyl group(C=N), while the signal at (123-137) ppm for aromatic carbons as shown as in fig. (12) .

Second step: The second step includes preparation of new six azetidinone compounds (B1-B6) (N-substituted-3-chloro-2- azetidinones) were prepared by reaction of chloro acetyl chloride with the prepared Schiff bases (A1-A6) in first step. The prepared compounds were characterized by physical properties, FT-IR, UV and some of them by ^{1}H-NMR , ^{13}C-NMR spectroscopy were recorded.



R= 

The synthesis of these compounds was carried out lined in scheme 1. And the physical properties for compounds (B1-B6) including melting point range of (102-239) ºC and %yield were ranged (57.5-70) and these compounds were identified by FT-IR, UV, ^{1}H-NMR and ^{13}C-NMR spectroscopy.

FT-IR spectrum of compounds (B1, B5) showed clear absorption bands at (1735, 1705) cm^{-1} respectively at tribute to (C=O) imide stretching frequency is good evidence for the success of this step of reaction while disappearance of υ (C=N) absorption bands at (1670, 1662)cm^{-1}respectivly in IR spectra of the products. The IR absorption bands are given in table (3) see fig.(3) and fig.(5).

In the ^{1}H-NMR spectrum of compound (B5) showed signals at (10.13) ppm was to (N-CH) proton , and multiples signal at (7.45-8.35) ppm due to aromatic protons , and singlet signet signals at (5.82) ppm due to (O-H) proton as shown in fig (13).

In the^{13}C-NMR spectrum of compounds (B5) showed signal at(162.8-165.2) ppm for carbonyl group(C=O), while the signal at (123-133) ppm for aromatic carbons as shown in fig.(14) , UV spectrum of compound (B2, B5) showed an absorption λ max at (272) nm, (277) nm which attributed to ($\pi-\pi^*$) as shown in fig (9) and fig (10).

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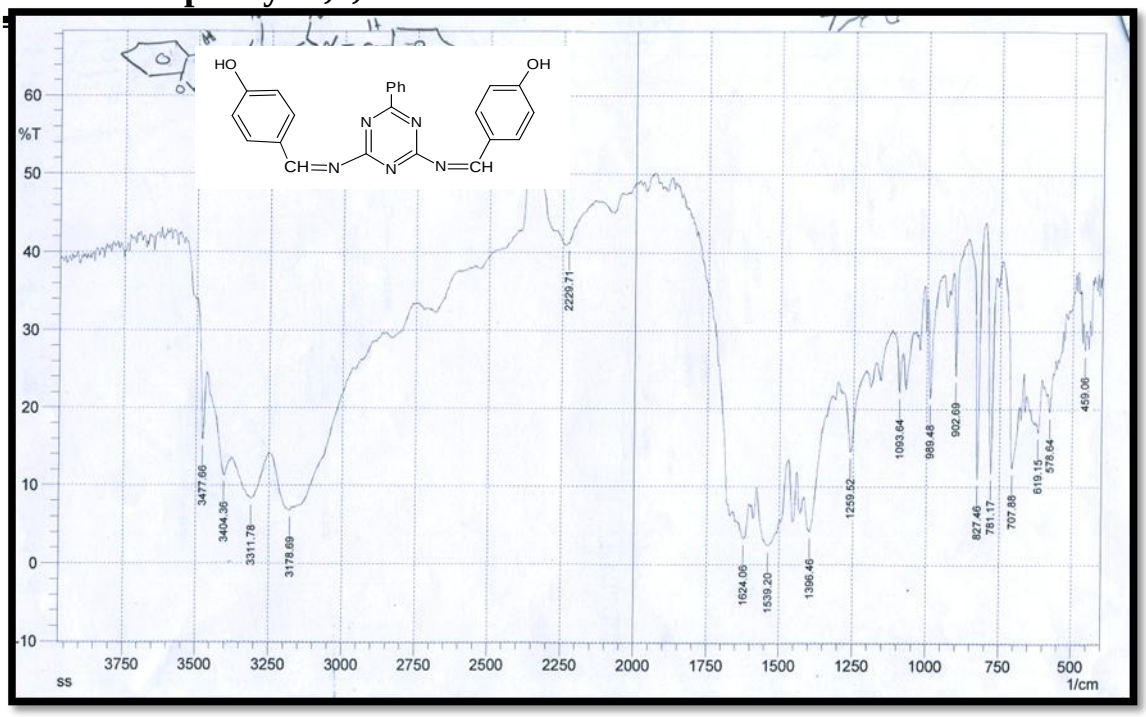

Fig (2): IR. Spectrum of Compound (A1)

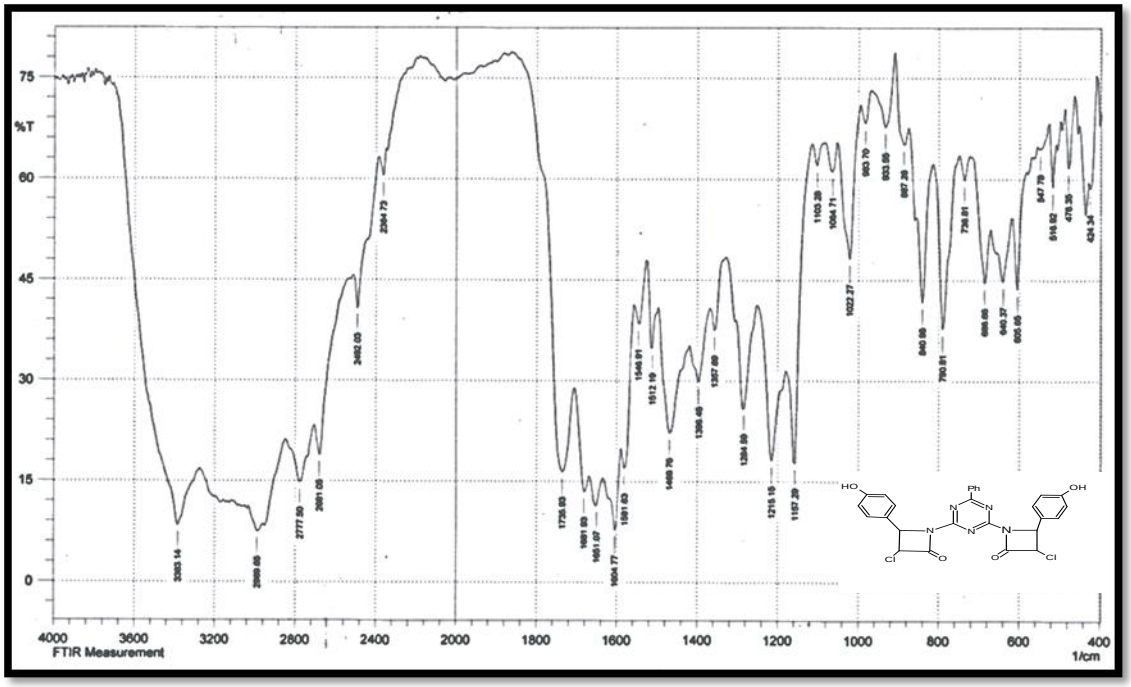

Fig (3): IR. Spectrum of Compound (B1)

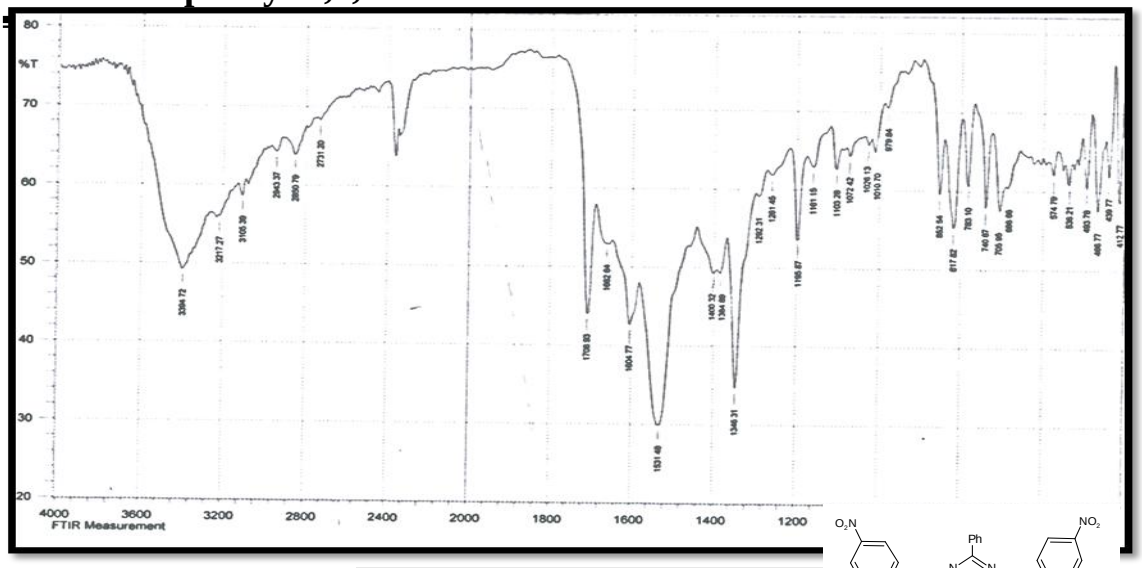

Fig (4): IR. Spectrum of Compoun

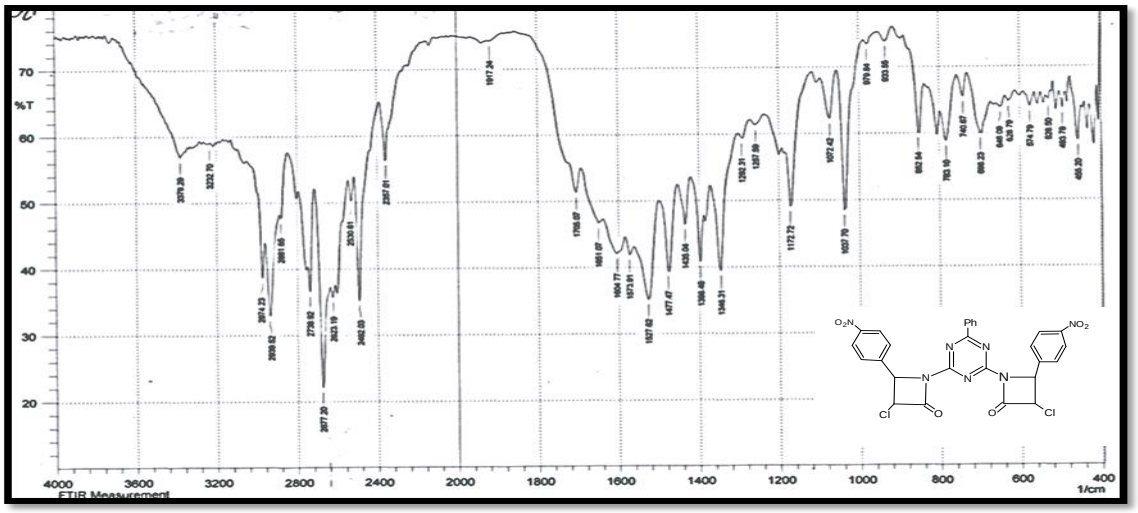

Fig (5): IR. Spectrum of Compound (B5)

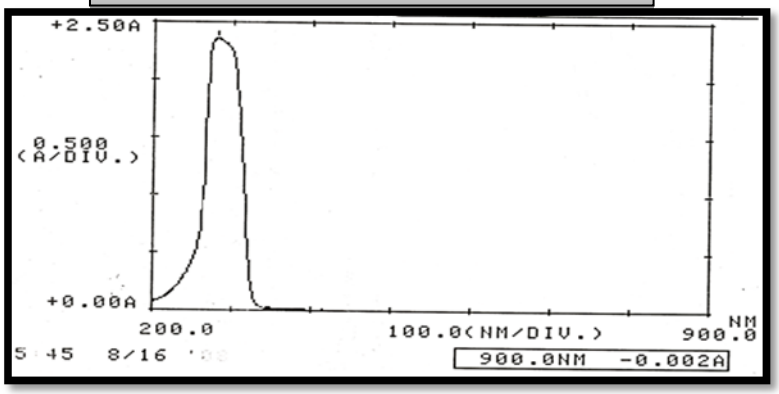

Fig (6): UV. Spectrum for the Original Compound

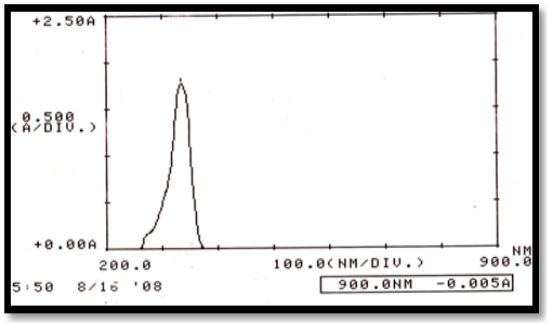

Fig (7): UV. Spectrum of Compound (A2)

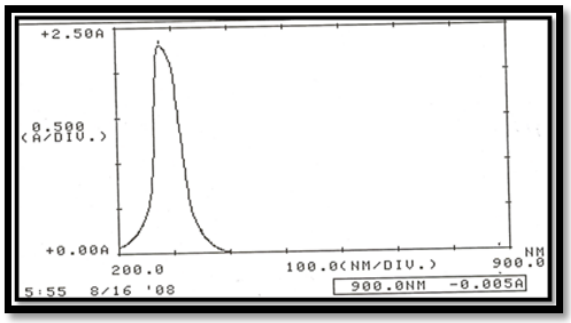

Fig (8): UV. Spectrum of Compound (A5)

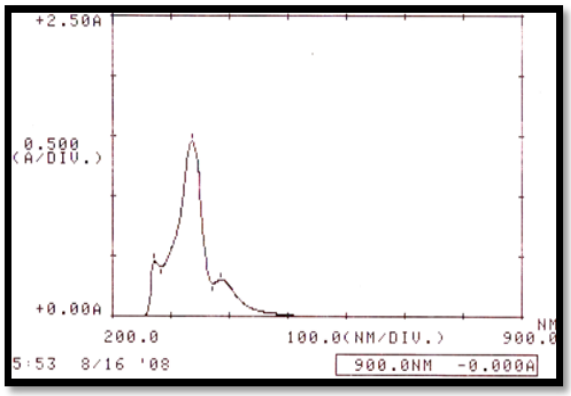

Fig (9): UV. Spectrum of Compound (B2)

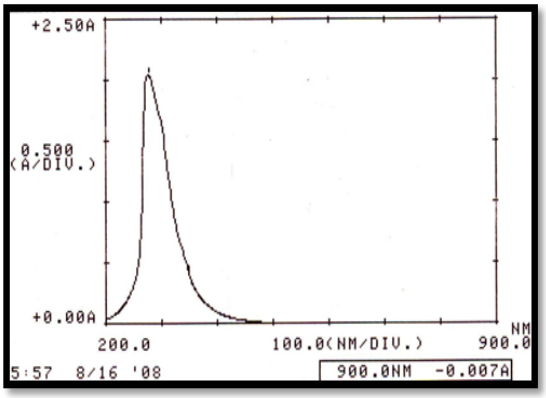

Fig (10): UV. Spectrum of Compound (B5)

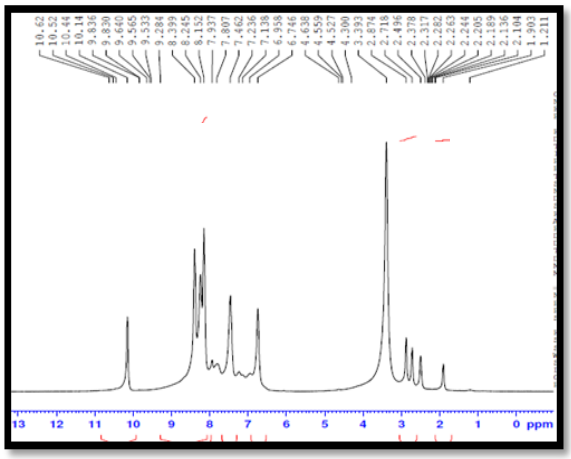

Fig (11)[1] H-NMR spectrum for Compound

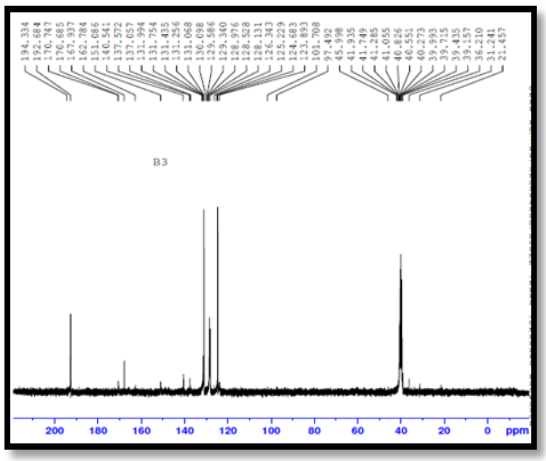

Fig (12)[13]C-NMR spectrum for Compound (A5)

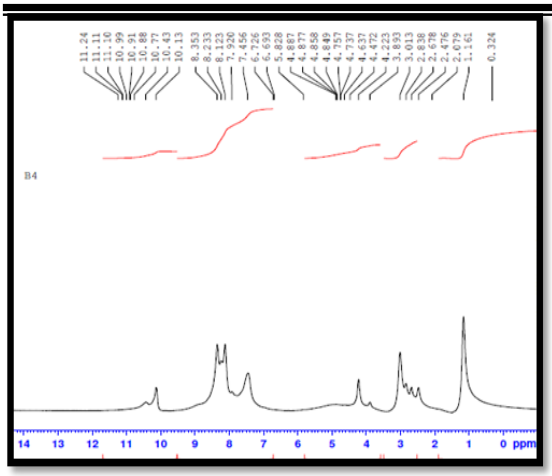

Fig (13)[1] H-NMR spectrum for Compound

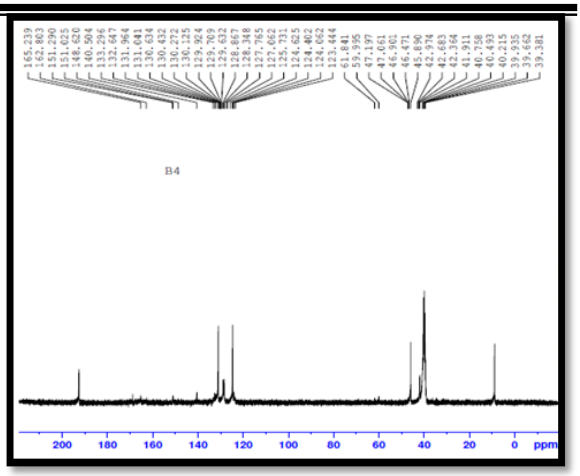

Fig (14)[13]C-NMR spectrum for Compound (B5)

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تحضير معوضات ٣-كلورو-٢- ازتيدينون لمشتقات ٤،٢-داي امينو -٦- فنيل ١ , ٣ , ٥- ترايزين

الخلاصة :

شملت الدراسة الحالية تحضير مركبات جديدة تحتوي على معوضات ٣-كلور-٢-ازتيدينون لمشتقات ٤،٢-داي امينو -٦- فنيل ١ , ٣ , ٥-ترايزين من خطوتين . حيث تضمنت الخطوة الاولى تحضير قواعد شف (A1-A6) من خلال تكثيف ٤،٢-داي امينو -٦- فنيـل ١ , ٣ , ٥- ترايزين مع العديد من الألديهايدات , ثم الخطوة الثانية تشمل إعداد ست مركبات ازتيدينون جديدة (B1 -B6) عن طريق تفاعل كلورو أسيتيل كلورايد مع قواعد شيف المعدة في الخطوة الأولى .المركبات المحضرة تم تشخيصها بأستخدم بعض الخصائص الفيزيائية مثل FT-IR والأشعة فوق البنفسجية وبعض منهما سجلت باستخدام طيف H-NMR, ^{13}C-NMR .