Synthesis and characterization of some heterocyclic compounds from 6-chloro-1,3-benzothiazole-2-thiol

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الخلاصة

في هذا البحث تم تحضير مشتقات حلقية غير متجانسة من ٦-كلورو ، ١,٣-بنزوثايازول -٢-ثايول وذلك بمفاعلة هذا المركب مع ٢-كلورو خلات الاثيل ليعطي المركب [1] ويتبعها مفاعلة الاخير مع الهيدرازين لينتج المركب [2] الذي بدوره سيدخل تفاعلات عديدة ليعطي سلسلة واسعة من المشتقات الحلقية الغير متجانسة حيث بتفاعله مع الديهايدات اروماتية مختلفة في مذيب الايثانول سيعطي قواعد شيف [3,4]، بغلق مركبات شيف باستعمال كلورو كلوريد الاستيل نحصل على مشتقات البيتا لاكتام [5,6] ، نحصل على مشتقات جديدة بتفاعل المركب [2] مع KOH,CS_2 سينتج المركب [7] الذي بدوره يتفاعل مع الهيدرازين ليعطي المركب [8] وبتفاعل الاخير مع الديهايدات اروماتية حلقية مختلفة نحصل على نوع اخر من قواعد شيف [9,10] ومن ثم الحصول على مركبات حلقية جديدة بتفاعل [9,10] مع ٢-مركبتو حامض الخليك لينتج [11,12] ثم مفاعلة المركب [2] مع ايزوثايوسيانات الفنيل لنحصل على المركب [13] ومن ثم يتم غلق المركب الاخير بواسطة NaOH لنحصل على مشتقات حلقية غير متجانسة جديدة [14] شخصت هذه المركبات بقياس درجة الانصهار والتقنيات الطيفية FTIR وبعضها شخص باطياف ^{1}H-NMR .

Abstract

This research involved some of heterocyclic derivatives from 6-chloro-1,3-benzothiazole-2-thiol by the reacted of this compound with chloro ethyl acetate to gave compound [1] in which reacted with hydrazine to gave compound [2] , the last compound will react with several reagents to gave a new series of heterocyclic derivatives in which compound [2] reacted with different aromatic aldehydes in ethanol to gave Schif bases [3,4] . The last compounds convert to β-lactam [5,6] by the reaction between Schiff bases and chloro acetyl chloride .

Compound [2] react with CS_2 ,KOH to gave a new derivative compound [7] in which reacted with hydrazine gave compound [8] and reacted with different aromatic aldehydes to gave another kind of Schiff bases [9,10] and cyclization of the last compound with 2-mercapto acetic acid to gave [11,12] .

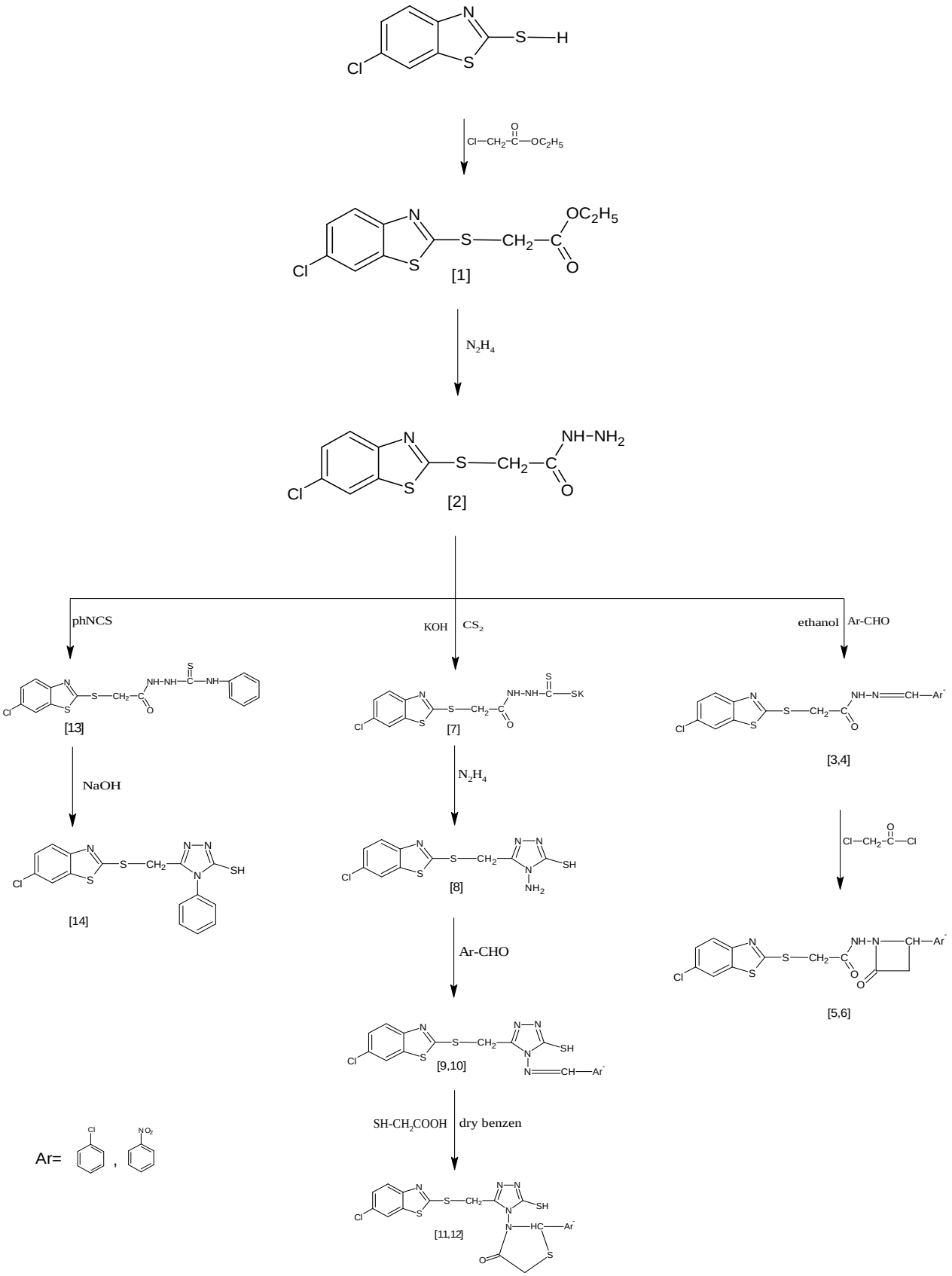
Reaction of compound [2] with phenyl isothiocyanate to gave compound [13] and cyclization of [13] by NaOH gave several new heterocyclic derivatives [14], these all compounds were characterized by their melting points, FTIR and ^{1}H-NMR spectra for some of them .

Key words : Chalcone , Pyrazole, Thiazine, Oxazine, Isoxazole

Introduction:

The triazole compounds are widely using in nature and take place in medicinal chemistry as drug intermediates[1]. They are clinically use in the metabolism of leving cells and the treatment of various diseases[2]. The triazole derivatives have been reported in the scientific literature[3]. Triazole ring having been used as antimicrobial agent and antihistamine[4] and it is use as diuretic[5] , anticonvulsant[6] , and anti inflammatory[7] . β-Lactam rings used as structural unit in the most widely antibiotics[8] , β-Lactam have been act as cholesterol acyl transfers inhibitors[9] , thrombin inhibitors [10] and cysteine proeas [11] . These antibiotics such as Ampicillin , Amoxicillin in which contained β-Lactam ring used for treatment of bacterial infection in both humans and food producing animals[12] .

Synthesis, characterization and structural activity of Schiff bases have been studied in which the linkage of C=N is very essential for bioactivity [13]. Schiff bases have been posses antibacterial[14] , antifungal[15] , anticancer[16] , ureas inhibition[17] , antioxidant[18] , antiglycation activities[19] and herbicidal activities[20]



Scheme 1: Synthesis of new compounds 1-14 from 6-chloro-1,3-benzothiazole-2-thiol.

Materials and Methods:

Instrumental:

The melting points were determined in open capillary tubes on a Gallen Kamp melting point apparatus and were uncorrected .The FTIR Spectra of some prepared derivatives were taken on Shimadzu FT-IR Spectra as KBr disc in AL-Mustansyria University , results are given cm^{-1} . ^{1}HNMR Spectra were recorded on Bruker Spectra Spin Ultra-Shield magnets 300MH_z instrument in Al Al-Bayt University /Jorden using DMSO-d^6 as solvent.

Experimental:

Preparation of ethyl [(6-chloro-1,3-benzothiazol-2-yl)sulfanyl]acetate [21][1]

In round bottom flask , (0.1mole) starting compound with (0.1mole) anhydrous potassium carbonate in the presence of (35ml)absolute ethanol mixed with stirring and then added (0.1mole) chloro ethyl acetate drop was to the mixture and reflux (10hr) . Evaporate the solvent and filter the mixture, the product we recrystallized from ethanol .Table (1)

Preparation of 2-[(6-chloro-1,3-benzothiazol-2-yl)sulfanyl]acetohydrazide [21][2]

A mixture of compound [1] (0.05 mol) and ethanol (30) was refluxed (2hr) then added excess of hydrazine hydrate (0.2mol) to the mixture and complete the reflux to (3hr). Then separated precipitate was filtered and recrystallized from ethanol .Table (1)

Preparation of Schiff bases [3, 4] general procedure:

Apreparate aromatic aldehydes (0.01mol) was added to a mixture of (0.01mole) of compound [2] in (40ml) absolute ethanol and 2-3 drops glical acetic acid the mixture was refluxed (5hr) and the product was filtered and recrystallized from suitable solvent .Table (1)

Preparation of β-Lactam compounds [5, 6] [22]:

Prepare a mixture of any kind of Schiff bases [3,4] (0.005mol) and (0.01mol) triethyl amine in (15ml) dioxin , Then add (0.005mol) chloro acytyl chloride drops to the mixture then the reaction was stirred for (10 hrs) . Was poured in to ice water , and the product was recrystallized from different solvent .Table (1)

Preparation of potassium 2-{[(6-chloro-1,3-benzothiazol-2-yl)sulfanyl]acetyl} hydrazine carbodithioate[23][7]

Prepare (0.01mole) from KOH with (30ml) ethanol solvent , another solution was prepared from (0.01mol) compound [2] with (0.01mol) CS_2 was added slowly to first solution and stirred overnight , after finishing the stirring , the dry ether (20ml) was added and yellow ppt. was filtered , washed with ether and vacuum dried .table (1)

Preparation of 4-amino-5-{[(6-chloro-1,3-benzothiazol-2-yl)sulfanyl]methyl}-4*H*-1,2,4-triazole-3-thiol [23][8]:

A mixture of (0.01mol) compound [7] in hydrazine hydrate (10ml) was refluxed until the colour of the mixture changed to green and homogenous solution resulted, cool the mixture and aciditified with (10%) HCl to yield the ppt. table (1)

Preparation of Schiff bases [23] [9, 10]:

A mixture of compound [8] (0.01mol) and aromatic aldehyde (0.01mol) in ethanol (20ml) was stirring with a few drops of glacial acetic acid at room temperature for about (7hr) ,then was heated at (70^0C) for (4hr) . After cooling the separated solid filtered and recrystallized from chloroform .Table (1)

Preparation of 1, 3-Thiazolidin-4-one derivatives [24][11,12]

(0.005mol) of any kind of Schiff bases [9,10] in (10ml) dry benzene with stirring , after that the mixture refluxed (12hr) the solvent distilled of and the residue neutralized with (10%)sodium bicarbonate , then was filtered and recrystallized by ethanol .Table 1)

Preparation of 2-{[(6-chloro-1, 3-benzothiazol-2-yl)sulfanyl] acetyl}-*N*-phenylhydrazine carbothioamide [23] [13]

Dissolve (0.01mol) of compound [2] in (20ml) ethanol and add (0.01mol) of phenyl isothiocyanate , the mixture was stirred at room temperature overnight , the ppt. was filtered and washed with ethanol . Table (1)

Preparation of 5-{[(6-chloro-1,3-benzothiazol-2-yl)sulfanyl]methyl}-4-phenyl-4*H*-1,2,4-triazole-3-thiol[23][14]

(0.005mol) of compound [13] with (0.005mol) of (25ml) sodium hydroxide (20%) was refluxed (8hr) , cooled , poured on to ice water , stirred and filtered . Table (1)

Table (1): Physical properties and FTIR data of prepared compounds

Comp. No.	M.P (C°)	Mol. formula	Yield %	FTIR (ν, cm^{-1})
1	175-177	$C_{11}H_{10}NO_2S_2Cl$	75	$(C-H)_{ar}$3113 , $(C-H)_{al}$ 2980 , $(C=O)_{ester}$ 1737 , (C-CL) 667 , (C-S) 603
2	220-222	$C_9H_8N_3O_2S_2Cl$	70	$(C-H)_{ar}$3039 , $(C-H)_{al}$ 2960 , $(C=O)_{ester}$ 1649 , (NH,NH_2) 3319,3200
3	155-157	$C_{16}H_{11}N_3OS_2Cl_2$	85	$(C-H)_{ar}$3034, (C = N) 1606, $(C=O)_{ester}$ 1626 , (NH) 3416, (C-CL) 650
4	135-137	$C_{16}H_{11}N_4O_3S_2$	55	$(C-H)_{ar}$3034, (C = N) 1606, $(C=O)_{ester}$ 1626 , (NH) 3416, (NO_2) 1344,1521
5	170-172	$C_8H_{13}N_3O_2S_2Cl$	65	$(C-H)_{al}$ 2983 ,$(C-H)_{ar}$3064, (C = O)lact 1716,$(C=O)_{ester}$ 1656 , (NH) 3464, (C-Cl) 649
6	150-152	$C_{18}H_{13}N_4O_4S_2$	60	$(C-H)_{al}$ 2983, (C = O)lact 1716, $(C=O)_{ester}$ 1656 , (NH) 3464, (C-Cl) 650, (NO_2) 1346,1508
7	salt	$C_{10}H_7N_3OS_4ClK$	78	-
8	170-172	$C_{10}H_8N_5S_3Cl$	60	$(C-H)_{ar}$3067 , (NH_2) 3481,3362 , (C = N) 1631,(C=S)1222
9	188-190	$C_{17}H_{11}N_5S_3Cl_2$	70	$(C-H)_{al}$ 2995 ,$(C-H)_{ar}$3067 , (C = N) 1624, (C-Cl) 628
10	122-124	$C_{17}H_{11}N_6O_2S_3Cl$	50	$(C-H)_{al}$ 2947 ,$(C-H)_{ar}$3067 , (C = N) 1626 , (C-Cl) 650 , (NO_2) 1344,1519
11	185-187	$C_{17}H_{11}N_5OS_4Cl_2$	65	$(C-H)_{al}$ 2980 ,$(C-H)_{ar}$3067, (C=O) 1750 ,

				$(NH)_{totumeric}$ 3419, (C-Cl) 619
12	220-222	$C_{17}H_{11}N_6O_3S_3Cl$	60	$(C-H)_{al}$ 2980 ,$(C-H)_{ar}$3067, (C=O) 1749 , $(NH)_{totumeric}$ 3419, (C-Cl) 619, (NO_2) 1379,1516
13	202-204	$C_{16}H_{13}N_4OS_3Cl$	55	$(C-H)_{al}$ 2966 ,$(C-H)_{ar}$3014, $(C=O)_{amid}$ 1614 , (NH) 3325, (C=S) 1219
14	253-255	$C_{15}H_{11}N_4S_3Cl$	60	$(C-H)_{ar}$3014, (C=N) 1645, $(NH)_{totumeric}$ 3479, $(C-H)_{al}$ 2962

Table (2):Chemical ^{1}H-NMR spectra of some compounds

Comp. No.	^{1} H- NMR (DMSO-d_6) ppm
2	7.22-7.94ppm (m, 3H, ArH), 9.45ppm (S,1H, NH), 4.65ppm (S,2H,NH_2)
6	6.37-8.21ppm (m, 4H, ArH), 4.1ppm (S,1H, NH), 5.0ppm (S,1H,$CH)_{Lactam}$
8	7.7-8.14ppm (m, 4H, ArH), 4.0 ppm (S,1H, SH), 4.5ppm (S,2H, S-CH_2), 7.5ppm (S,2H,NH_2)
14	6.96-7.53ppm (m, 9H, ArH), 4.46ppm (S,2H, S-CH_2), 12.3ppm (S,1H,NH)

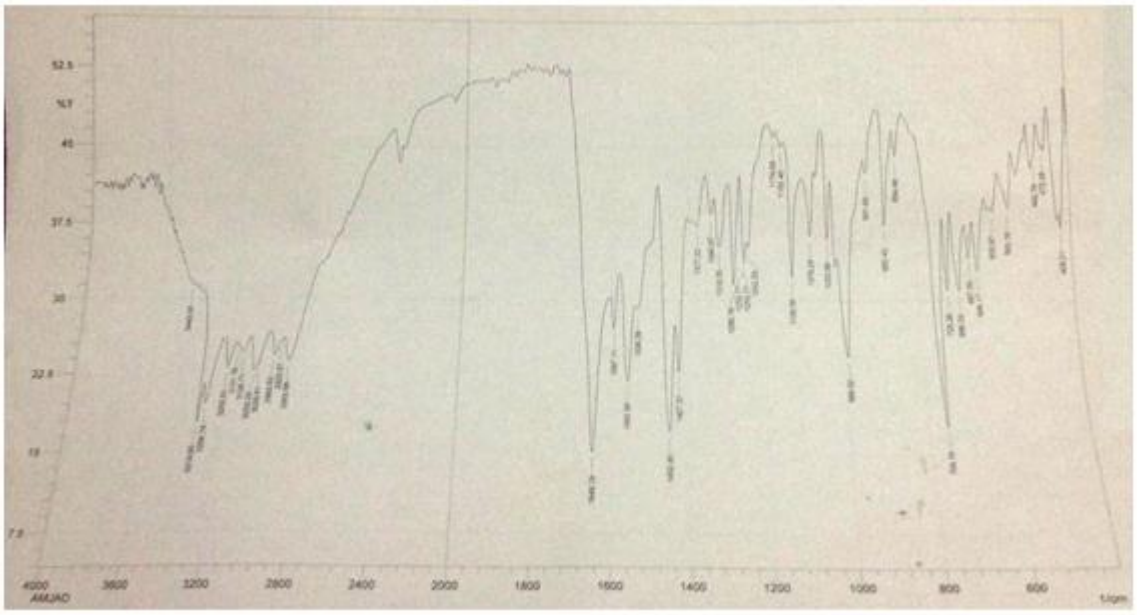


Figure 1: FT-IR spectrum of compound 2 .

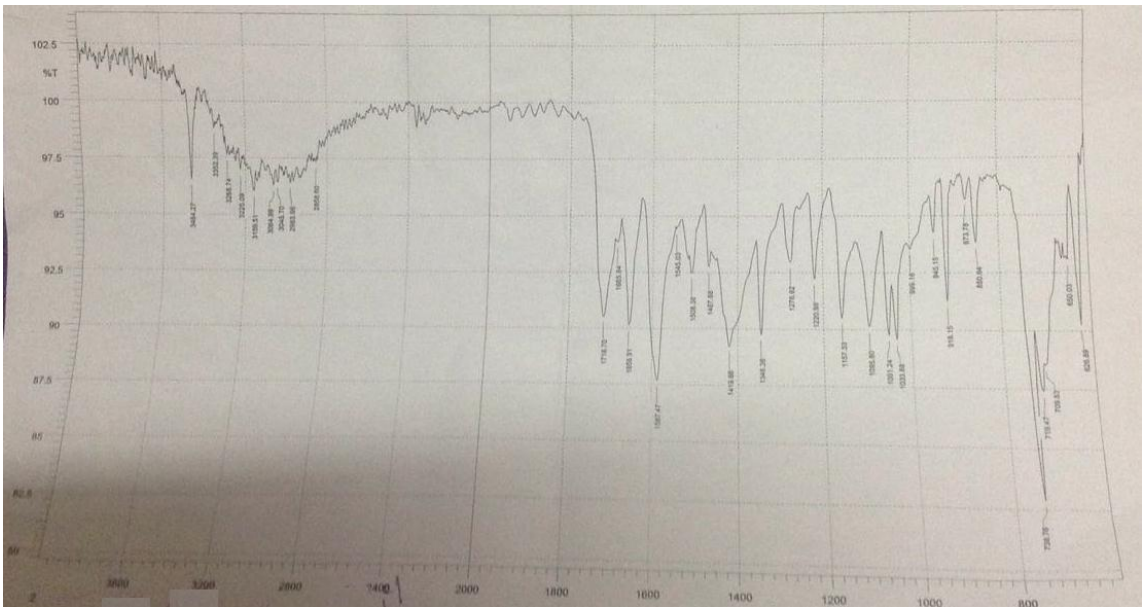


Figure 2: FT-IR spectrum of compound 5 .

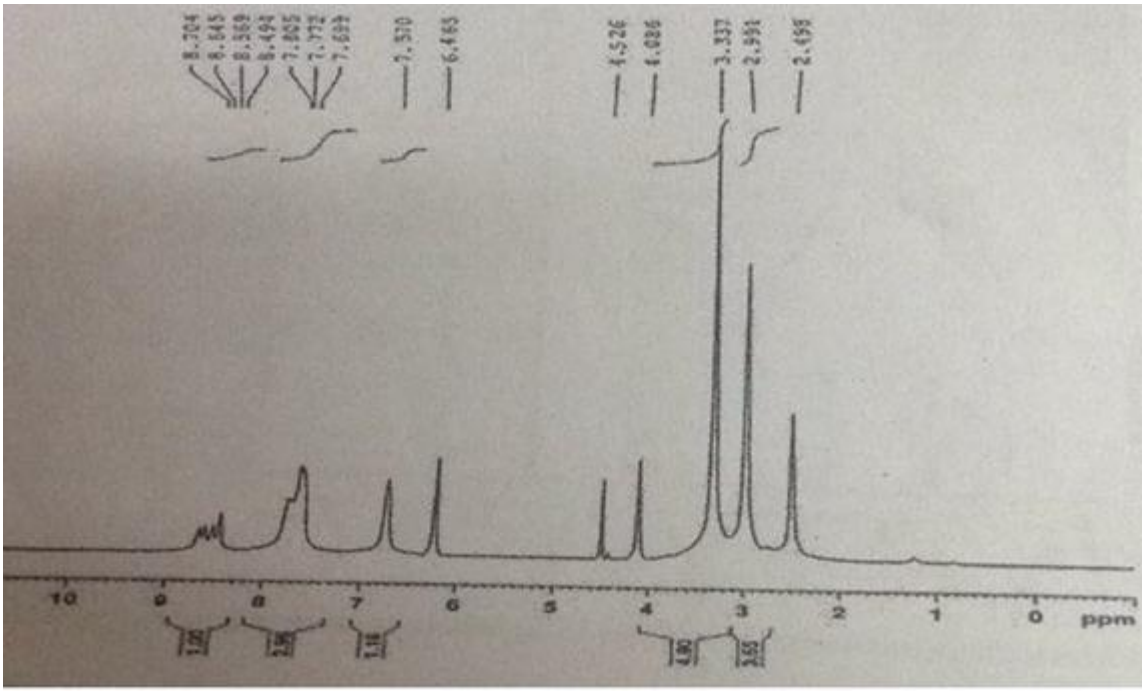


Figure 3: ^{1}H-NMR spectrum of compound 8 .

Results and Discussion :

The reaction sequence for the preparated compounds out lines in scheme1

As we seen that the compound [1] was prepared by the reaction between 6-chloro-1,3-benzothiazole-2-thiol and chloro ethyl acetate , the structure of compound [1] was characterized by its FT-IR spectra through the appearance of (C=O)ester at 1737cm^{-1} . The treatment of compound [1] with hydrazine hydrate produced compound [2] in with the (C=O) ester was shift to 1649cm^{-1} and the (-NHNH$_2$) bands appearance at (3319,3200)cm^{-1} .

When we react compound [2] with appropriate aromatic aldehyde by using ethanol as solvent produced compound [3,4] which called Schiff bases in which we recognized the is compounds by appearance of azomethine (C=N) stretching band at 1606cm^{-1} with keeping the appearance of (C=O)ester at 1626cm^{-1} and disappearance of (NH$_2$) band .

After the preparation of Schiff bases we reacted this compounds in cyclization reaction between Schiff basses [3,4] with cloro acetyl chloride in presence of triethyl amine and dioxin solvent to produce compounds [5,6] called β-Lactam derivatives we recognized the product compound by the bands at (1716,1720)cm^{-1} due to (C=O) Lactam.

In schem we found the reaction between compound [2] with CS_2 in the presence of KOH would product the salt compound [7] in excellent yield , in which then cyclized by refluxing with hydrazine hydrate to give compound [8] which characterized it by the appearance of NH_2 bands at (3981,3362)cm^{-1} related with triazole ring , we use this compound to prepare another kinds of Schiff bases [9,10] which cyclized by the using of 2-mercapto acetic acid to yield compound [11,12] recognized them by the appearance of the carbonyl thiazolidine at (1749,1750)cm^{-1}.

As shown in scheme that compound [2] was condensed with phenyl isothiocyanate to produced compound [13] , the FT-IR of the compound show the disappearance of NH_2 band and they appearance of NH band at (1614)cm^{-1} and (C=S)band at (1219)cm^{-1} ,after the reaction of compound [13] with NaOH we obtained on compound [14] which appeared band at (3479)cm^{-1} due to the totumeric form for (NH) .

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