Synthesis and Characterization of Novel Schiff Bases of Imide Moiety

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Abstract

In our research novel schiff bases of imides moiety have been synthesized . Novel Schiff base derivatives of imides moiety have been synthesized by multistep reaction . First step involves prepare 2-amino -5-mercapto-1,3,4-thiadiazole (I) by the cyclization of thiosemicarbazide with carbon disulphide and anhydrous sodium carbonate in ethanol as a solvent . Then , compound (I) was reacted with phthalic anhydride in the presence of glacial acetic acid to give 2-(5-mercapto-1,3,4-thiadiazol-2-yl) isoindoline-1,3-dion (II).Compound (II)was heated with ethyl chloracetate in the presence of potassium carbonatproduced ethyl 2-(5-(1,3-dioxoisoindoline -2-yl)-1,3,4-thiadiazole-2-yl thio) acetate (III).The reaction of compound (III) with hydrazine hydrate yielded 2-(5-(1,3-dioxoisoindoline -2-yl)-1,3,4-thiadiazol-jm2-ylthio)acetohydrazide (IV).The fifth step involves reaction of compound (IV) with N,N-dimethyl aminobenzaldehyde to yield N´-(4-(dimethyl amino)benzylidene)-2-(5-(1,3-dioxoisoindoline-2-yl)-1,3,4-thiadiazole-2-yl-thio)acetohydrazide (V).The structures of the newly synthesized compounds were confirmed by physical properties and spectral (FT-IR,^{1}H-NMR)analysis

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KeyWords:2-(5-(1,3-dioxoisondolin-2-yl)-1,3,4-thiadizole-2-yl thio)acetohydrazide , phthalic anhydride , Schiff bases.

* This paper is extracted from master thesis of the first author .

Introduction

Imides are the biologically active compounds having different pharmacological activities such as analgesic ,anti-inflammatory ,anti-microbial ,anti-depressant and anti-cancer etc. These compounds play an important role in medicinal chemistry in drug development and drug discovery . Cyclic imide moiety and their derivatives play an integral part in various important molecules such as thalidomide ,isogranulatimide and rebeccamycinetc . These are the compounds which possess various pharmacological activities such as analgesic ,anti-inflammatory , anti-depressant and anti-viral etc[1-7] .

The discovery and development of schiff basesof imide moiety are the most powerful technology . A heterocyclic compounds plays an important role in regulating the biological activities . Schiff bases contain carbon –nitrogen double bonds in which nitrogen atom get linked to aryl and alkyl atoms . Schiff bases can possess different pharmacological activities and also have industrial applications .Schiff bases of imides possess different pharmacological activities such as antimicrobial ,anti-inflammatory, antidepressant ,antipyretic etc[8-9]

Natural and synthetic macrocycles continue to attract extensive scientific interest, with research developments proceeding in many directions including anion receptors , molecular recognition , drug discovery , therapeutics and nanoscience [10] .

Macrocyclic systems have evolved from the original crown ethers spherands , cryptands and prophyrins , through calixarenes , resorcinarenes , rotaxanes , catenanes and beyond, as wellas into interdisciplinary fields and biological applications [11] .

Experimental

A-Materials

All the chemical used in the synthesis were of analytical grandes .

B – Instrumentation

Melting points were recorded using electro thermal melting point apparatus and are uncorrected . Infrared spectra were recorded as KBr disc on SHIMADZU-FT-IR-8400 spectrometer.^{1}H-NMR spectra was recorded on Bruker 300 MHz instrument using DMSO-d^{6} as a solvent and TMS as internal reference,measurement were made at Al-Albayt University. Jordan . . the progress of the reaction was monitored by TLC using aluminum silica gel plates .

Synthesis of 2- amino - 5- mercapto-1,3,4- thiadiazole (I) [12] .

A mixture of (2 gm , 0.02 mol.) of thiosemicarbazide and (2.33gm,o.o2 mol.) of anhydrous sodium carbonate were dissolved in 25 ml. abs .ethanol .To this solution (3.2 gm,0.04 mol.) of carbon disulphide was added . The resulting mixture was heated under reflux for 10 h . The reaction mixture was then allowed to cool down at room temperature . Most of solvent was removed under reduced pressure and the residue was dissolved in 20 ml .distilled water , carfefully acidified with cold conc . hydrochloric acid to give pale yellow precipitate . The crude product was filtered and washed with cold water , recrystallized from hot water to give the desired product as yellow needles , yield (75%), m.p (230-232)c^{o}.

Synthesis of 2-(5-mercapto- 1,3,4-thiadiazole -2-yl) isoindoline -1,3-dione (II) [13] .

To a solution of 2- amino -5- mercapto 1,3,4-thiadiazole (0.01mol.) in ethanol (20 ml.) .phthalic anhydride (0.01mol.) and acetic acid were added drop by drop, the solution was stirred magnetically for 2h at room temperature and then reaction mixture was refluxed for 6 h, then the mixture was allowed to stirring for one hour at room temperature . The mixture was poured on distilled water .The product was filtered , washed by hot water and recrystallized from acetone . yield (93%), m.p (266-268)c^{o}.

Synthesis of Ethyl 2-(5-(1,3-dioxoisoindoline-2-yl)1,3,4-thiadiazole-2 -yl-thio) acetate (III) [14] .

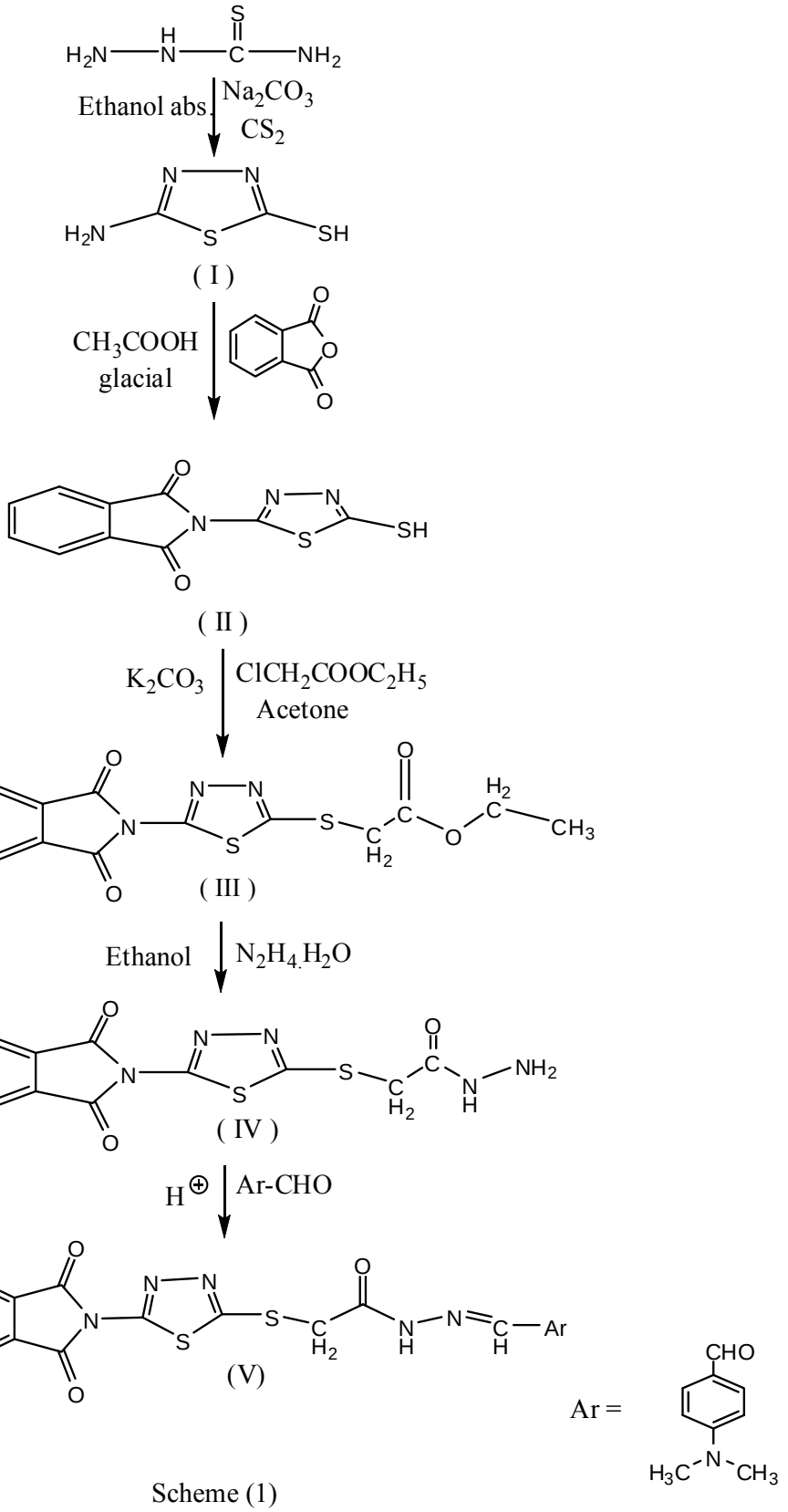
Ethyl chloroacetate (0.01 mol.) was added drop wise to a hot solution of compound (II) and potassium carbonate in acetone as a solvent .The mixture was refluxed for 4h .and allowed to stand .Evaporating the solvent under reduced pressure , water was added and the crude product was extracted with ethyl acetate and dried over anhydrous magnesium sulphate .Evaporating of the organic layer gave solid products , recrystallized from ethanol . yield (60%) , m.p (119-120) c^o.

Synthesis of 2-(5-(1,3-dioxoisoindoline-2-yl)-1,3,4-thiadiazole-2-yl-thio) acetohydrazide (IV) [14] .

To a hot solution of hydrazine hydrate (0.01 mol) in ethanol (10 ml) a solution of compound (III) in ethanol (10 ml) was added and the mixture was reflux for 6 h . The mixture was allowed to cool and the precipitate was filtered ,dried and recrystallized from ethanol . yield (88 %) , m.p (209-212)c^o .

SynthesisofN´-(4-(dimethylamino) benzylidene)-2-(5-(1,3-dioxoisoindolin-2-yl)-1,3,4-thiadiazol-2-yl-thio)acetohydrazide (V) [14].

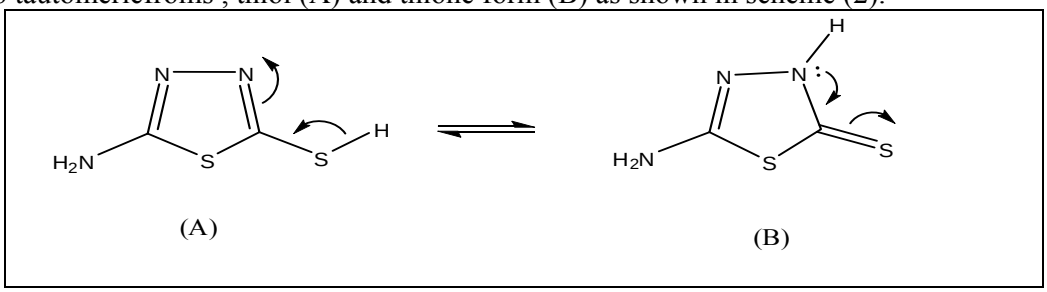
A mixture of compound (IV) (0.01 mol) and N,N-dimethyl aminobenzaldehyde (0.01 mol) in absolute ethanol was refluxed for 6 h .then the mixture was cooled . The solid product was filtered , dried and recrystallized from ethanol . yield (31 %) , m.p (215-217)c^o.


Ethanol abs.
Na2CO3
CS2
(I)
CH3COOH
glacial
(II)
K2CO3
ClCH2COOC2H5
Acetone
(III)
Ethanol
N2H4.H2O
(IV)
H⊕
Ar-CHO
(V)
Ar =

Scheme (1)

Results and Discussion

Compound (I) 2-amino-5-mercapto-1,3,4-thiadiazole was prepared through the reaction of thiosemicarbazide with carbon disulphide in the presence of anhydrous sodium carbonate in absolute ethanol .The structure of compound (I) was identified by its melting point and FT-IRspectroscopy.The FT-IR spectrum of compound (I)[15], figure (I) shows the following characteristic bands , two bands at 3396 cm^{-1} and 3277 cm^{-1} were due to asymmetric and symmetric stretching vibration of ($-NH_2$) group respectively , an absorption band at 3093 cm^{-1} was due to the (N-H) stretching (tautomeric form).The (-SH) stretching band found as very weak shoulder at 2331 cm^{-1} , a band at 1604cm^{-1} was due to (C=N) stretching of the thiadiazole ring moiety . The sharp band at 1533 cm^{-1} and 1330 cm^{-1} are due to the (N-H) bending and (C-N) stretching vibration respectively . Also , the absorption band at 1055 cm^{-1} for the (C=S) group which gives an evidence that compound (I)can exist in two tautomericfroms , thiol (A) and thione form (B) as shown in scheme (2).



Scheme (2)

The second strategy used in the present work involved treatment of phthalic anhydride with 2-amino-5-mercapto-1,3,4-thiadiazole in glacial acetic acid under reflux condition for many hours . Structure of this compound (II)was confirmed by FT-IR and ^{1}H-NMR. FT-IR spectra of compound (II),figure(2) showed disappearance of absorption bands belong to ($-NH_2$) amine at (3396-3277)cm^{-1} . Also , FT-IR spectra showed many clear absorption bands including band at (1735-1786)cm^{-1} , (1602)cm^{-1} , (1544)cm^{-1} , (1354-1363)cm^{-1} due to (C=O)imide , (C=N) ,(C=C) , (C-N) imide and (C-S) respectively .^{1}H-NMR spectrum of compound (II),figure(3) showed signals at δ(3.33 ,2.33,7.96 -8.04 ,14.66) ppm due to amine proton ,SH, aromatic protons and NH tautomer [16] .

Compound (III) was synthesized by the reaction of compound (II) with ethyl chloroacetate in the presence ofanhydrus potassium carbonate in acetone . FT-IR spectrum of compound (III),figure(4) showed appearance of absorption band at 1749 cm^{-1} due to carbonyl group of ester [17] .

^{1}H-NMR spectrum of compound (III) ,figure (5) , shows the following characteristic chemical shifts (DMSO-d^6,ppm):the aromatic ring protons appeared as multiplies atδ(7.60 , 8.05) ppm. Single signal (4.30) ppm due to the ($-CH_2-S-$) group [18].Triplet signal atδ (1.21) ppm for the methyl group and the guartet signal at (4.13) ppm for the methylene group . Compound (IV) was synthesized by the reaction of compound (III) with hydrazine hydrate in ethanol absolute , the compound was identified by FT-IR and ^{1}H-NMR spectra .The FT-IR spectra of compound (IV), figure (6)showed disappearance of carbonyl group at 1749 cm^{-1} and appearance band at 3415-3267 cm^{-1} due to ($-NH_2$) group and at 1660 cm^{-1} for carbonyl group of amide.The^1 H-NMR data of compound (IV) ,figure (7)shows the following characteristic chemical shifts (DMSO-d^6 ,ppm): the aromatic ring proton appeared as multiplies at δ(7.53-8.07)ppm and at 3.96 (s,2H,of SCH_2), 11.5 (br. s,H of NH amide), 3.34 (br. s,2H of NH_2) [19].

The condensation reaction of equimolar quantity of compound [IV] with aromatic aldehyde was the major method to prepare schiffsbases .FT-IR spectrum of compound (V) , figure (8) ,

showed the disappearance of two absorption bands at 3415- 3267 cm^{-1} due to the (-NH_2) stretching of amino group , and appearance of band at 1654 cm^{-1} due to (C=N) group of imine .^{1}H-NMR was more informative , characteristic peaks were observed atδ(6.69-8.17) (mult ,H of two benzene ring) , 4.05 (s,2H,of SCH_2), 2.67 (s,6H, of $N(CH_3)_2$), 11.38 (s,1H,of NH of amide), 4.43(s,1H,CH=N).

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Table No. (1):physical properties of prepared compounds

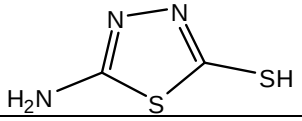
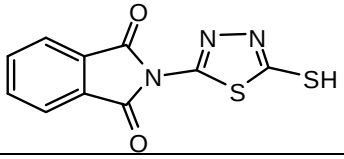
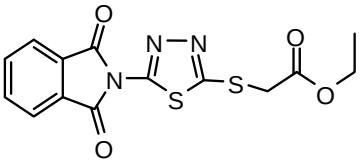
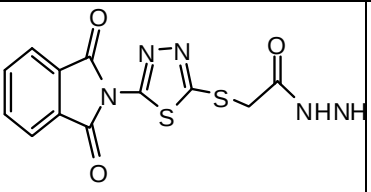
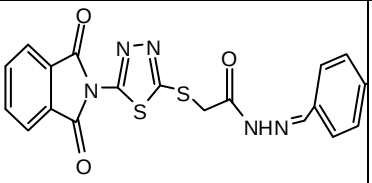
Com. No.	Molecular formula	Structural formula	M.p .C°	Recrystallized solvent	color	Yield %
1	$C_2H_3N_3S_2$		230-232	Water	yellow	75
2	$C_{10}H_5O_2S_2$		266-268	Acetone	Dark Yellow	93
3	$C_{14}H_{11}N_3O_4S_2$		119-120	Ethanol	Brown	60
4	$C_{12}H_9N_5O_3S_2$		209-212	Ethanol	white	88
5	$C_{21}H_{18}N_6S_2$		215-217	Ethanol	Pale yellow	31

Table No.(2):FT-IR Spectral data of the prepared compounds

Comp. No.	FT-IR spectral data cm^{-1}						
	C-H aromatic	C-H aliphatic	(C=O) imide	(C=N)endo., exo.	(C=O)amide, ester	(C=C) arom.	(N-H)amine, amide
I				1604			3396 3277 3174
II			1735 1786	1602		1544	3199
III	3099 3068	2985 2953 2900	1724 1793	1608	1749 ester	1550	
IV	3018	2980 2899	1724	1600	1660 amide	1558	3415 3267 3167
V	3016	2968 2918 2899		1600 endo. 1654 exo.	1662 amide	1558	3167 3120

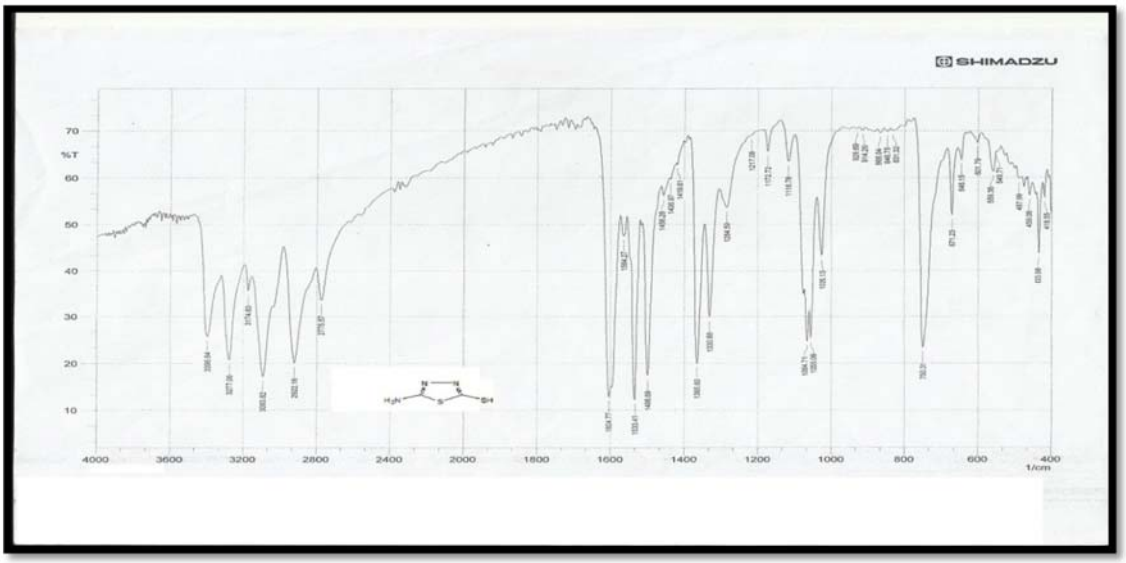


Figure No.(1):FT-IR spectrum of compound (I)

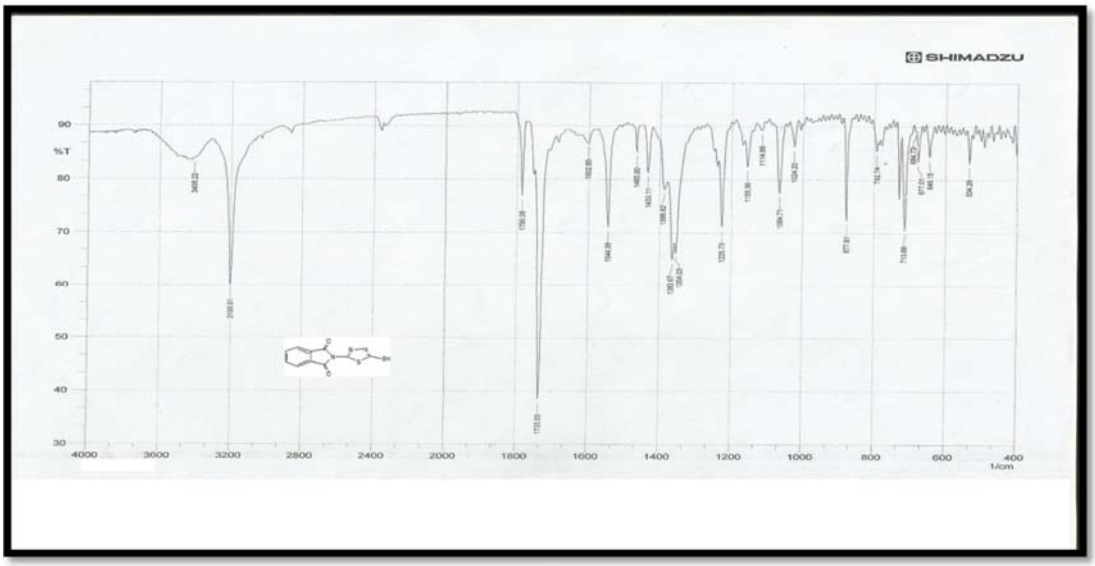


Figure No.(2):FT-IR spectrum of compound (II)

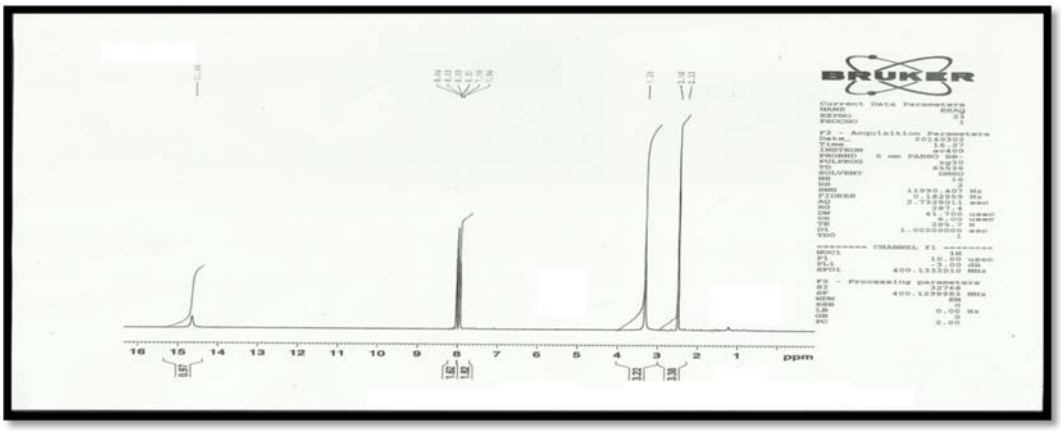


Figure No.(3):1H-NMR spectrum of compound (II)

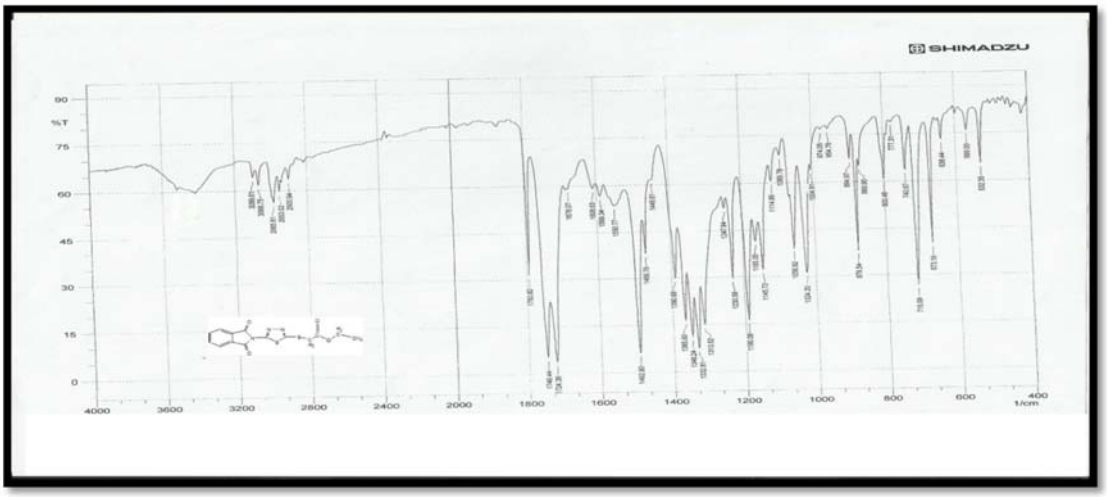


Figure No.(4):FT-IR spectrum of compound (III)

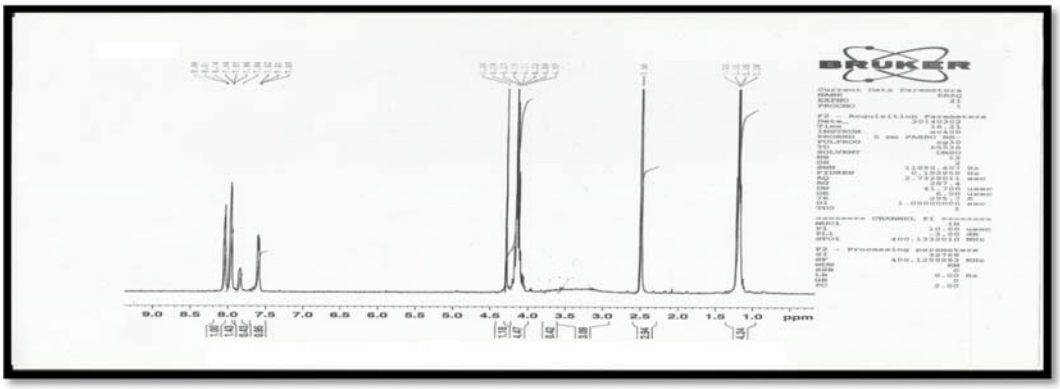


Figure No.(5):1H-NMR spectrum of compound (III)

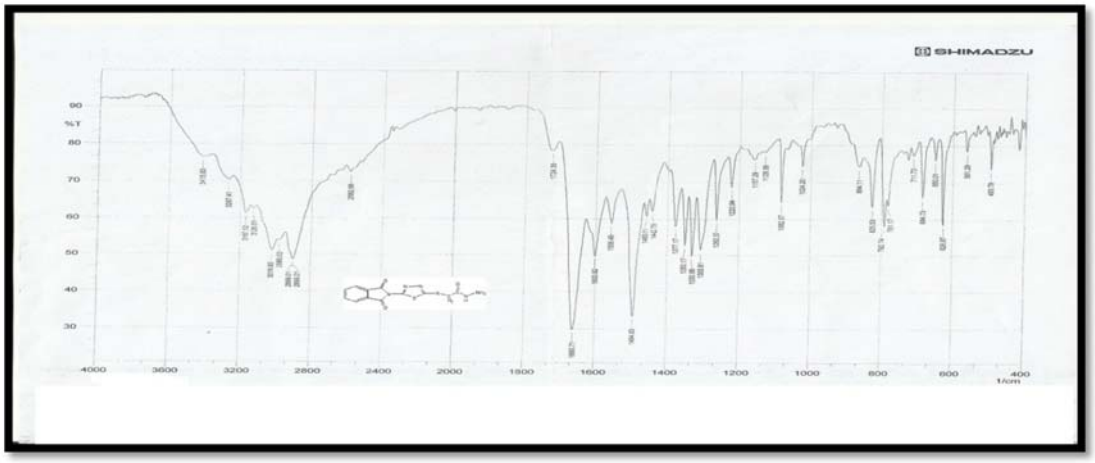


Figure No.(6):FT-IR spectrum of compound (IV)

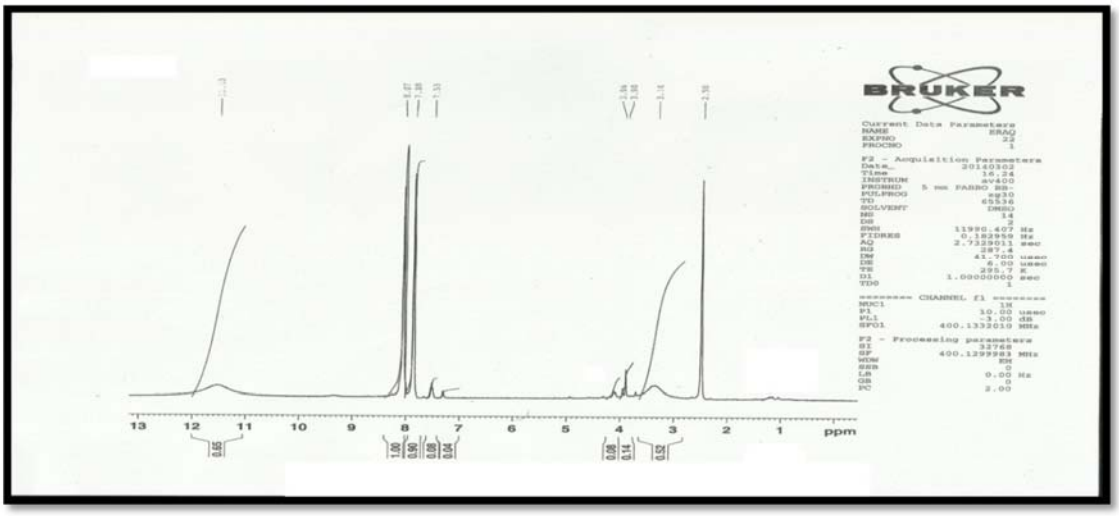


Figure No.(7):1H-NMR spectrum of compound (IV)

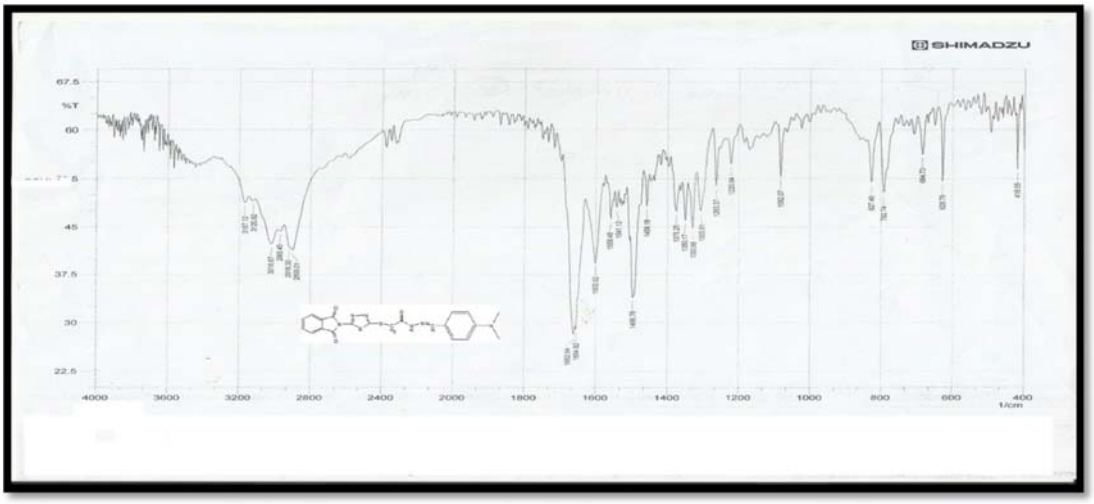


Figure No.(8):FT-IR spectrum of compound (V)

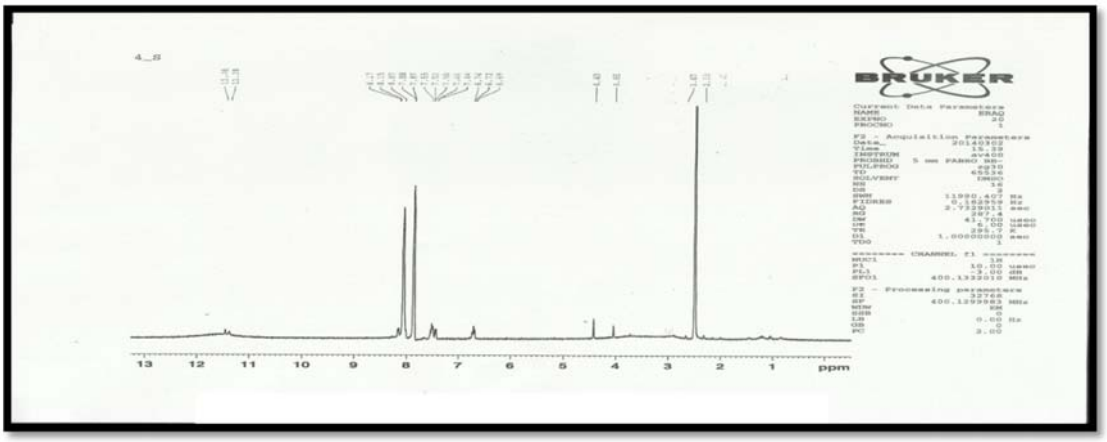


Figure No.(9):1H-NMR spectrum of compound (V)

تحضيروتشخيص قواعد شف جديدة لوحدة الامايد

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استلم البحث في:22 نيسان 2014 , قبل البحث في:29 ايلول 2014

الخلاصة

في بحثنا هذا تم تحضيرقواعدشف جديدةتحتوي على الايمايد .مشتقات قواعد شف الجديدة والحاويه على الايمايد حضرت بتفاعل متعددالخطوات . تضمنت الخطوةالاولى تحضيرالمركب 2- امينو 5- مركبتو -1,3,4- ثياديازول (I) بتحولق الثايوسيمكارباز ايد مع ثنائي كبريتيدالكاربون بوجود كاربونات الصوديوم اللامائيه وفي مذيب كحولي , بعدذلك تفاعل هذا المركب مع انهيدريدالفثاليك بوجود حامض الخليك الثلجي ليعطي 2-(5- مركبتو- 1,3,4-ثياديازول-2-يل) ايزواندولين-1,3- ثنائي – ون (II) . المركب (II) تفاعل مع خلات كلوريدالاثيل بوجود كاربونات البوتاسيوم ليعطي 2-(5-(1,3- ثنائي اوكسوايزواندولين -2- يل)-1,3,4- ثياديازول -2- يل ثايو) استيت (III) . تفاعل المركب(III) مع الهيدرازين هايدريت ليعطي 2-(5-(1,3- ثنائي اوكسوايزواندولين -2- يل)1,34, - ثياديازول-2- يلثايو) اسيتوهايدرازايد (IV) . الخطوةالخامسةتضمنتتفاعلالمركب (IV) معN,N-ثنائي فثلامينوبنزلديهايد ليعطي4)-N´-ثنائي مثيل امينوبنزلدين)-2-(5-(3,1 – ثنائي اوكسوايزواندولين-2-يل)-1-3-4 ثياديازول-2-يل ثايو)اسيتوهايدرازايد (V) .
تراكيب المركبات المحضرةالجديدة شخصت من خلال الخواص الفيزيائية وتحاليل اطياف (^{1}H-NMR , FT-IR) .

الكلمات المفتاحية:2-(5-(1,3- ثنائياوكسوايزواندولين -2- يل)-1,3,4- ثياديازول -2- يل ثايو) استيت,انهدريدالفثالك,قواعد شف