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SYNTHESIS AND CHARACTERIZATION OF NEW COMPOUNDS DERIVATIVES FROM 2-MERCAPTO - 5- CYANO-1,3,4-THIADIAZOLE AND STUDY OF ITS BIOLOGICAL ACTIVITY

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ABSTRACT:

The work involves preparation many compounds which derivatives from 5-Cyano-2-mercapto compound react with ethyl bromo acetate in presence of Sodium ethoxide as a strong base will be give Ethyl [5-Cyano(1,3,4-thiadiazole-2-yl)thio]acetate and when the last allow to react with hydrazine will be product[5-Cyano(1,3,4-thiadiazole-1-2-yl) thio]aceto hydrazide which condensation with carbonyle compounds to give Schiff ' bases.
All compound have testing by biological activity for tow concentration (10^{-4},10^{-6})M on some kinds of bacteria.

INTRODUCTION:

The synthesis of compounds 1,3,4-thiadiazole rings has been attracting widespread attention due to the divers pharmacological properties such as antimicrobial,anti in fammatory,analgesic and antitumoral activities [1-7].In addition, several 1,3,4-thiadiazole derivatives have been reported to posses divers biological activities although there are a number of anti biotics which are commercially used in medicine the synthesis of new increasing drug resistance [8-12].Morever, it is important to obtain therapeutical compound having less toxic effect[13].
In addition it was reported that 1,3,4-thiadiazole exhibit various biological activities possibly due to the presence of the =N-C-S mioety[14].
All aldehydes & ketone(aliphatic or aromatic) have the ability to condensation with primary amine (aliphatic or aromatic) or amine acid in order to give compounds called imines which contain isomethin group[15-16].
In last years schiff's bases aquired a big attention as abeneficial drug materials according to biological activities which prove it [17].Some them as becteriostatic, and the other show cardio vascular activity, also many of it show anti tubercular activity and antifungal activity.[18]

Eperimental section:

Melting points were determined on a Gallen kamp MFB-600 point apparatus and are uncorrected.The U.V spectra were measured by instrument" Shimadzu U.V –visible double beam scaning spectrophotometer-260).Whil IR spectra were measured as potassium bromide pellets using two instrument that "Pye-Unicam SP3-100 spectrophotometer-which have the range 600-4000) and shimadzu FTIR 8000 series Test scan.

Preparation of ethyl[5-Cyano(1,3,4-thiadiazole)-2-yl)thio]acetate.(1).

(0.01mole) from 5-Cyano-2- mercapto thiadiazole was refulxed with an equivalent amount of sodium in absolute

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ethanol for 2 hours .Then ethyle bromo acetate(0.01 mole) was added and refluxed for an additional 5 hours. Having evaporated it, brown crystals appeared. This was recrystallized with ethanol 50%.

Preparation of [5-Cyano(1,3,4-thiadiazole)-2-yl] thio aceto hydrazide(2);

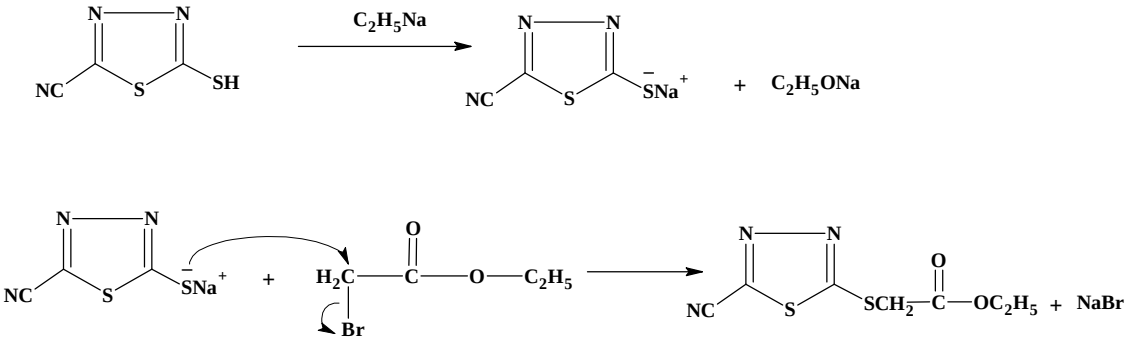
To solution of corresponding compound (0.01) mole in 50 ml absolute ethanol,hydrazine was added and refluxed this mixture for five hours, then having evaporate to get green crystallized with ethanol 50%.

Synthesis of Schiff bases (3-7):

(0.01mole)from compounds (2) was refluxed with an equivalent amount of keton or aldehydes in the presence absolute ethanol for three hours,then cooled to 0C°.The precipitate filtered off and recrystallized with ethanol 50% and table 3 show some of physical properties of compounds.

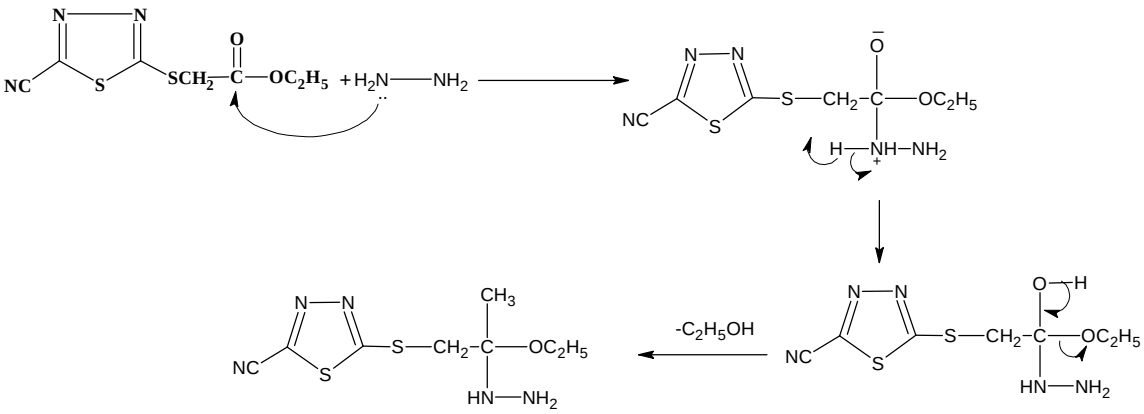
RESULT & DISCUSSION:

Compounds (1) "5-cyano(1,3,4-thiadiazole)-2-yl) thio acetate prepared from the reaction between 5-Cyano-2-mercapto (1,3,4-thiadiazole with ethyl bromoacetate in the presence of solution sodium ethoxide which the last will draw the proton from mercapto group ,then the acetate group will be replace the proton to get compound (1) as the following mechanism.



The IR spectrum of compound (1) showed many absorption bands,One of them appearing at 1735 cm^{-1} attributed too carbonyl group of ester and another observede at 1612cm^{-1} due to C=N of thiadiazole ring and two bands at 2923cm^{-1} 2975 attributed to C-H aliphatic,observable absent the band at 2760cm^{-1} which due to SH group and absorption at 1268cm^{-1} which due to C=S . U.V spectrum showed two beak, one at 332nm due to $\pi \rightarrow \pi^*$ and at 202nm due to $n \rightarrow \pi^*$. Hydrazide's derivatives one of more important compounds which have biological activity.It can be considered as usfull intermediated leading to the formation of some heterocyclic ring such as 1,2,4-triazole-3-thion and 1,3,4-oxadiazole [19].One of widespread methods for preparation hydrazides that the reaction of ester with hydrazine in ethanol , and this reaction consider one of nucleophilic substitution reactions which submit to the tetrahedral mechanism[20].

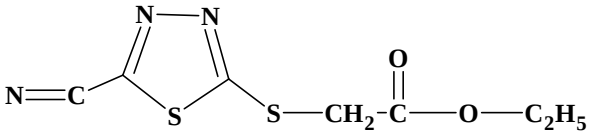
The treatment of compounds(1) with hydrazine produce compound (2). In the initial stage of this reaction hydrazine molecule should be attack ester carbonyl to give unstable molecule intermediate compound which suffuring elimination of ethanol group to give hydrazide's derivatives as show in the following mechanism.



In IR spectrum of compound (2) displayed the C-O absorption at 1115 cm^{-1} beside additional NH_2 absorption at 3430cm^{-1} and absorption band of C=O of amide at 1680cm^{-1},all this absorption bands verified the converted ester to hydrazide's derivative. U.V spectrum showed absorption at 235 nm due to n→π* and at 360 due to π→π*.

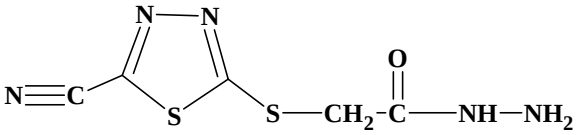
All schiff's bases prepared by condensation of hydrazine or hydraide compounds with aldehydes or keton.The reaction involves neucleophilic attack for amine group avoid carbonyl group for aldehydes or ketone to form N-Substituted hemiaminals followed by elimination water molecule to give stable compound.

Tables: Table (1-a) show some of physical prpoperties of compound(1) which have the chemical structure



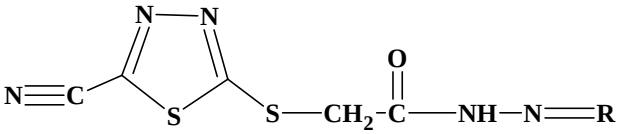
Comp.No.	M.P.C°	Yeild %	Recrystalization
1	٩٥	75	EtOH 50%

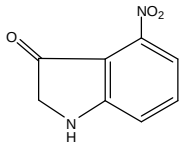
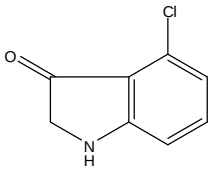
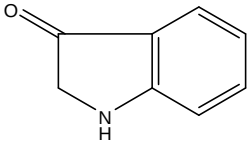
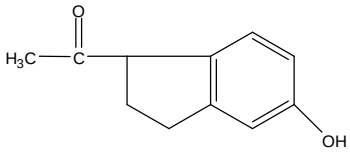
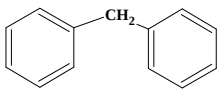
Table(1-b):show some of physical properties of compound(2) which have the chemical structure.



Comp.No.	M.P.C°	Yeild	Recrystalization
2	110	70	EtOH 50%

Table (1-c) show some of physical properties of compounds which have the chemical structure.



	R	M.PC°	Yeild	Recrystallization
3		**142**	**85**	**Ethanol 50%**
4		**145**	**82**	**=**
5		**149**	**78**	**=**
6		**153**	**75**	**=**
7		**187**	**77**	**=**

Table(2-a) show bands of IR spectra for compound(1)

Comp.No.	U.V EtOH λ_{max}	ν(CH)cm^{-1} aliph	C=N	C=O For ester	Others cm^{-1}
1	332 202	2975 2923	1612	1735	C-O for ester 1115

Table(2-b) showed bands of IR spectra for compound(2).

Comp.No.	U.V EtOH λ_{max}	ν(CH)cm^{-1} aliph	C=N	C=O For ester	Others cm^{-1}
2	235 360	2920 2970	1012	3430 3450	C=O of amide 1680

Table(3) show the bands of I.R spectra of compounds(3-7).

Comp. No.	U.V EtOH λ_{max}	ν(CH)cm^{-1} aliph. cm^{-1}	ν(CH)cm^{-1} arom. cm^{-1}	ν C=N cm^{-1}	ν C=C	Others cm^{-1}
3	350 231	2920	3105	1640 Interference with C=N of H.C.S	1530 Interference with NO2	C=O Esatin 1710
4	205 333	2922	3095	1630 Interference with C=N of H.C.S	1540	C-Cl 750cm^{-1} C=O esatin 1708
5	204 310	2910	3097	1620 Interference with C=N of H.C.S	1535	C=O of estin 1700
6	229 335	2980	3100	1632 Interference with C=N of H.C.S	1530	-OH phenol 3610 ν(C-O) 1205 Para substituted ion 850
7	220 335		3100	1625 interference	1545	

Synthesis And Characterization Of New Compounds Derivatives From 2-Mercapto -5- Cyano-1,3,4-Thiadiazole And Study Of Its Biological Activity

جدول رقم (١) وضعت عينات الاسنان المسوسة في (Trypton Soy Broth) لمدة ساعتين ثم زرعت على (Macconkey)، (Blood Agar) فظهرت في اليوم التالي (Streptotococcus viridans)
٢- (distilled water) لمدة ساعتين ... وبنفس الطريقة رقم(١) فظهرت نفس النتائج اعلاه مع فارق ان رقم (١) النمو اكثر كثافة.

Wells method														disc Method													
g	f	e	d	c	b	a	7	6	5	4	3	2	1	g	f	e	d	c	b	a	7	6	5	4	3	2	1	Bacteria
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	S 12 mm	R	R	S 13 mm	R	S 14 mm	R	R	R	S 15 mm		Escherichi coli
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	Streptococcus
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	Staphy locus aureas
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	S	S	Photous stylomenella
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	S	R	Klebsie Spp

R = Resist
S= Sensitive
mm = millimeter inhibition zone region
1-7 with Concentration with 10^{-4}
a-g= 1-7 with concentration 10^{-6}

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Synthesis And Characterization Of New Compounds Derivatives From 2-Mercapto -5-Cyano-1,3,4-Thiadiazole And Study Of Its Biological Activity

تحضير وتشخيص مركبات جديدة مشتقة من ٢-مركبتو-٥-سيانو-١،٣،٤-ثايادايازول ودراسة فعاليتها البايولوجية.

د.عزيز عباس* ، ساجدة منادي ثامر*

الخلاصة :

يتضمن هذا البحث تحضير عدد من المركبات المشتقة من المركب (5-Cyano -2- mercapto-1,3,4-thiadiazole) والذي يتفاعل مع (ethyl bromo acetate) بوجود (Sodium ethoxide) كقاعدة قوية ليعطي (Ethyl[5-Cyano(1,3,4-thiadiazole 2-yl)thio]acetate) والاخير عندما يتفاعل مع الهيدرازين يعطي مشتقات الهيدرازايد (5-(Cyano(1,3,4-thiadiazol)-2-thio]aceto hydrazide) والتي تتكاثف مع مركات الكاربونيل لتعطي قواعد شيف.

جميع المواد المحضرة تام اختيار الفعالية البايولوجية لها بالتركيزين (10^{-4}M, 10^{-6} M) وعلى بعض انواع البكتريا المسببة لتسوس الاسنان.

*** قسم الكيمياء الحياتية / كلية الطب / جامعة ذي قار**