Fayoum University

Faculty of Science

Chemistry Department

“Synthesis and reactions of some heterocyclic compounds Containing Nitrogen and Sulphure”

By

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Summary

This thesis describes the studying of the behavior of ,6-amino-4-(4-chlorophenyl)-3,4-dihydro-2H-thiopyran-3,5-dicarbon -itrile(IIa) ,6-amino-3,4-dihydro-4-(4-methoxyphenyl)-2H-thiopyran -3,5-di-carbonitrile (II b), towards some electrophiles and nucleophiles to produce some compounds have expected antimicrobial activates.

The thesis consists of the following parts:

1) Summary

2) Introduction:

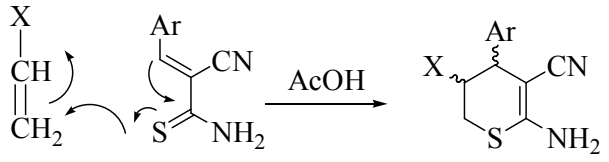
In this section brief literatures review of the different methods of preparation and the reactions of thiopyran derivatives.

3) Discussion:

It deals with the discussion of the experimental methods adopted for the synthesis of the designed compounds as well as the result of different analytical methods applied for the characterization of the new compounds.

Schemes 1-15 illustrate the synthetic pathways followed in the preparation of the target compounds.

In this part the author synthesis 6-amino-4-(4-chlorophenyl)-3,4-dihydro-2H-thiopyran-3,5-dicarbonitrile(IIa),**II b-d** also by reaction between 2-cyano-3-aryl prop-2-enethioamide and acrylonitrile or ethyl acrylate in refluxing acetic acid to produce thiopyran derivatives **II a-d**.



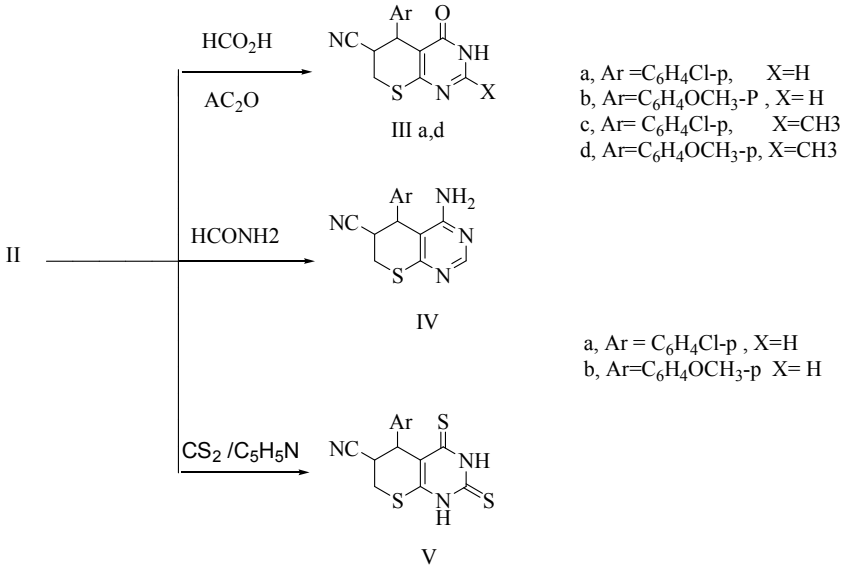
I II

a = C_6H_4Cl-p
b = $C_6H_4OCH_3$-p

a = C_6H_4Cl-p, X = CN
b = C_6H_4OCH3-p, X = CN
c = C_6H_4Cl-p, X = CO_2Et
d = $C_6H_4OCH_3$-p, X = CO_2Et

Scheme 1

1- Compounds**II a,b** react with different reagents namely: formic acid, formamide, carbon disulfide, and acetic anhydride afforded the fused thiopyranopyrimidines **IIIa-d, IVa**,**b,Va,b**respectively (Scheme 2)

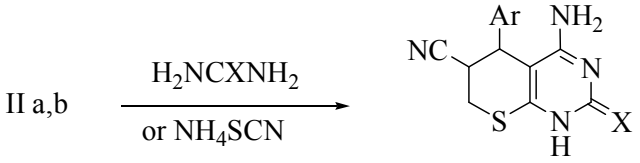


a, Ar =C_6H_4Cl-p, X=H
b, Ar=$C_6H_4OCH_3$-P , X= H
c, Ar= C_6H_4Cl-p, X=CH3
d, Ar=$C_6H_4OCH_3$-p, X=CH3

a, Ar = C_6H_4Cl-p , X=H
b, Ar=$C_6H_4OCH_3$-p X= H

Scheme 2

2- Reaction between **II a,b** and thiourea , urea and ammonium thiocyanate in acetic acid gave thiopyranopyrimidines **VI a-d**(Scheme 3).



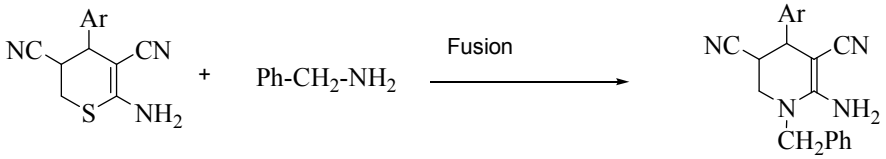
VI a-d

a, Ar=C_6H_4Cl-p,
b, Ar=$C_6H_4OCH_3$ -p; X= O

c, Ar=C_6H_4Cl-p,
d,Ar= $C_6H_4OCH_3$-p; X=S

Scheme 3

3- Fusion of II **a,b** with benzyl amine gave pyridine derivatives **VIII a,b**.

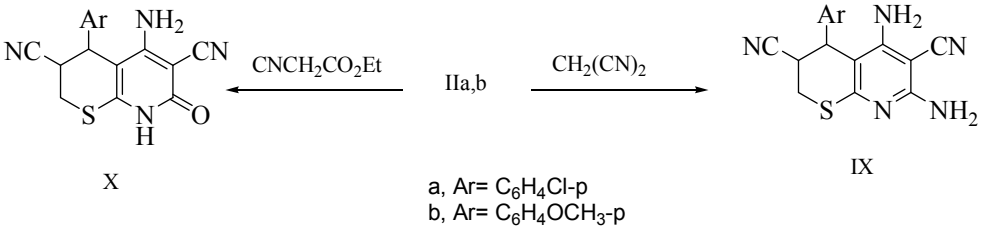


VIII

a=Ar, C_6H_4Cl-p
b=Ar, $C_6H_4OCH_3$-p

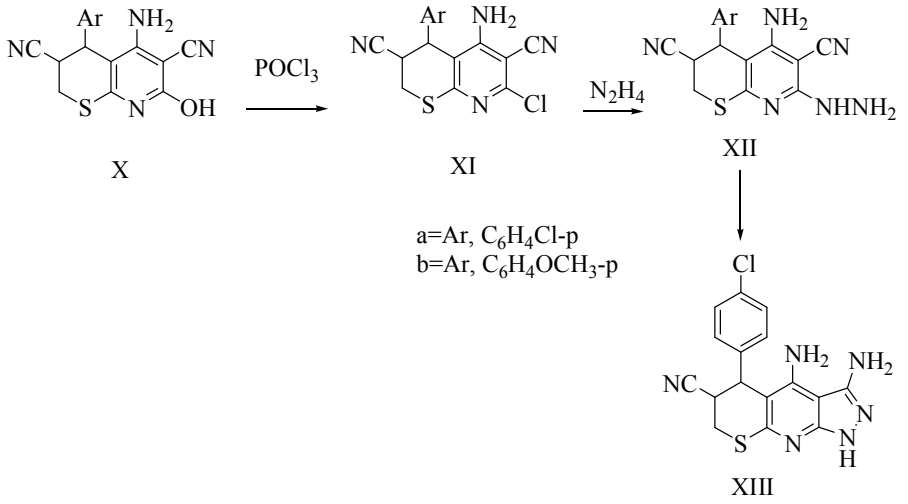
Scheme 4

4- Reaction of **IIa,b** with each of Malonitrile. andethyl aceto -acetate in Ethanol affordedthiopyranopyrindine derivatives **IX, X, a,b**.



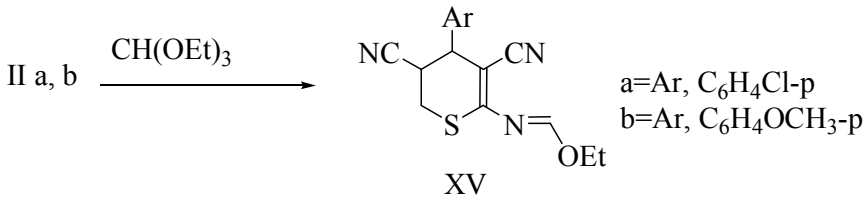
Scheme 5

5- Reaction of Compound**X a,b**with$POCl_3$ followed by reactionwith hydrazinehydrate and cyclization withHClgave(Scheme 6).



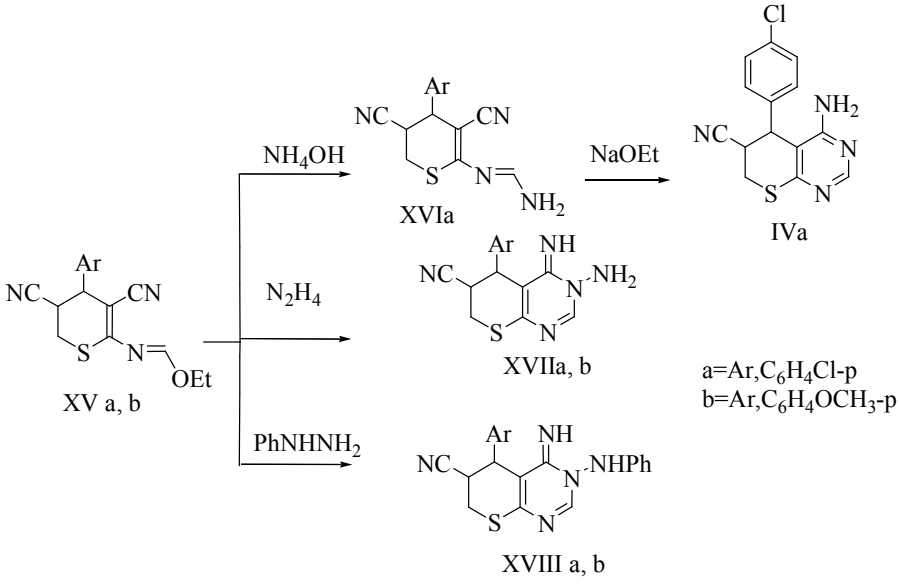
Scheme 6

7-Compounds **II a,b**, reacted with triethylorthformate in the presence of acetic anhydride in pyridine to giveethoxy methylene amino derivatives **XVa,b**.



Scheme 7

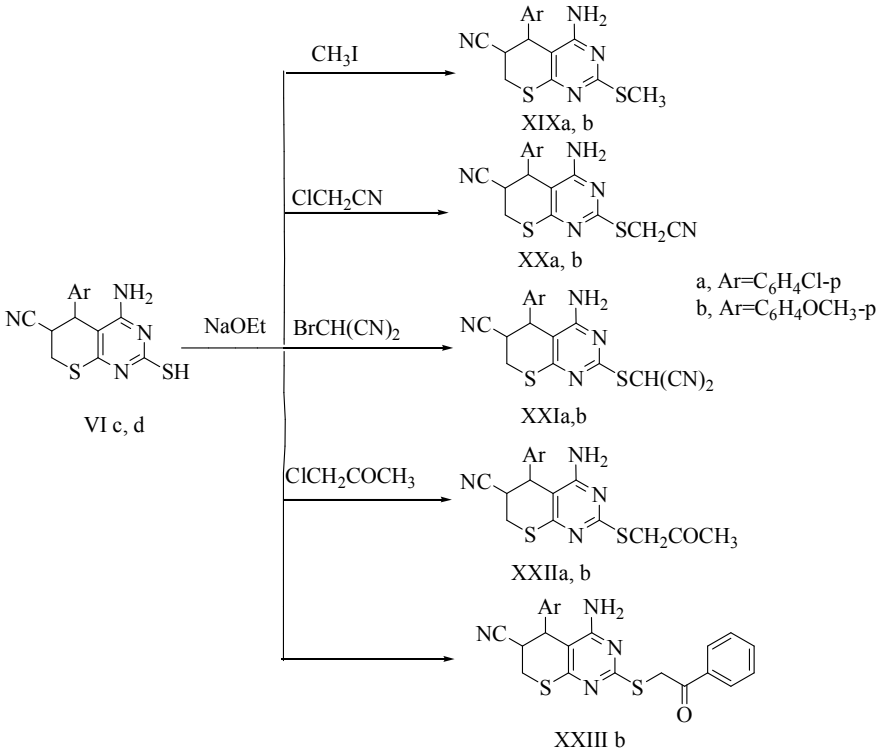
8- Reaction of **XV** with each of ammonium hydroxide, hydrazine hydrate and phenyl hydrazine in boiling ethanol, according to Scheme 8,gave thiopyrano -pyrimidines derivatives **XVI a, XVII a,b,** and **XVIIIa,b**.



Scheme 8

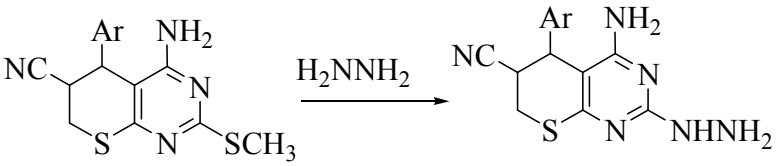
9- Reaction of compound **VI c,d** with α-halocompounds, namly methyl iodide, phenacyl bromide, chloro acetone, monobromo malonitrile, and chloroaceto- nitrile in sodium ethoxide

solution afforded S- alkylated compounds **XIXa,b-XXIIIa,b** respectively (scheme 9).



Scheme 9

10-Compound **XIX a,b** reactedwith hydrazine hydrateto yield **XXIV a,b**.

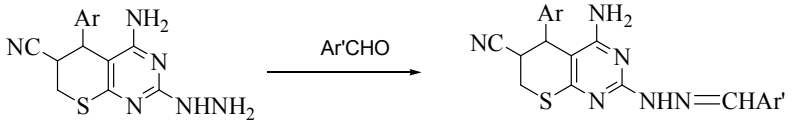


XIXa,b XXIVa,b

a,Ar= C_6H_4Cl-p
b,Ar= $C_6H_4OCH_3$-p

Scheme 10

11- To get a new series of expected biologically active compounds, it was of interest to condense hydrazine Compounds **XXIV a,b** with different aromatic aldehydes namely, benzaldehyde, p-Chlorobenzaldehde, and p-methoxy -benzaldehdein acetic acid to give the corresponding Schiff's bases **XXVa-f** respectively.(Scheme11).



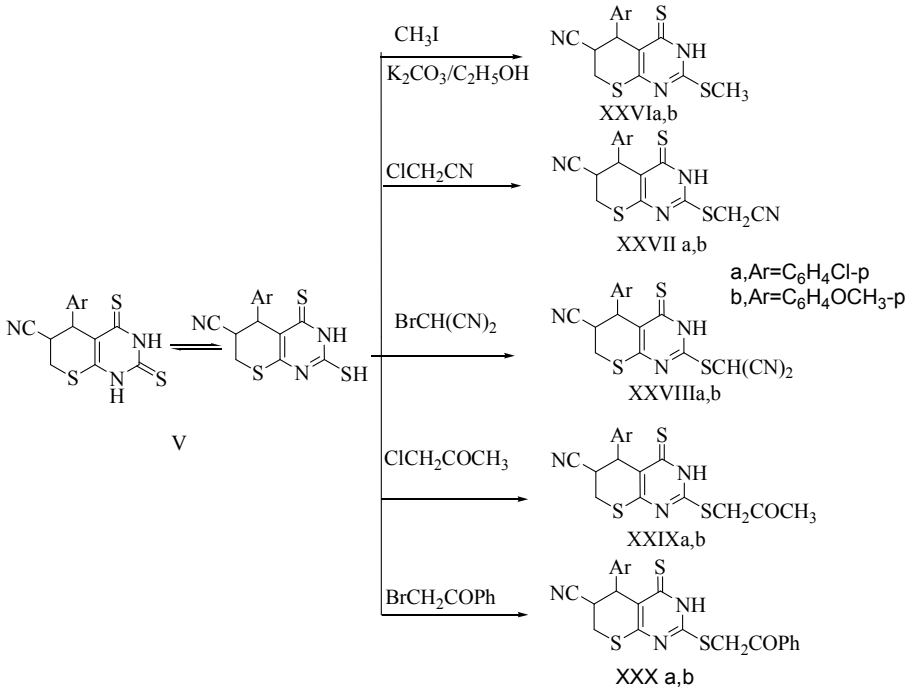
XXIVa,b

XXVa-f

a,Ar= C_6H_4Cl-p ; Ar' = C_6H_4
b, Ar=Ar'= C_6H_4Cl-p
c,,Ar= C_6H_4Cl-p ; Ar' = $C_6H_4OCH_3$-p
d,Ar= $C_6H_4OCH_3$-p ; Ar' = C_6H_4
e,Ar= $C_6H_4OCH_3$-p ; Ar' = C_6H_4Cl-p
a,Ar= Ar'= $C_6H_4OCH_3$

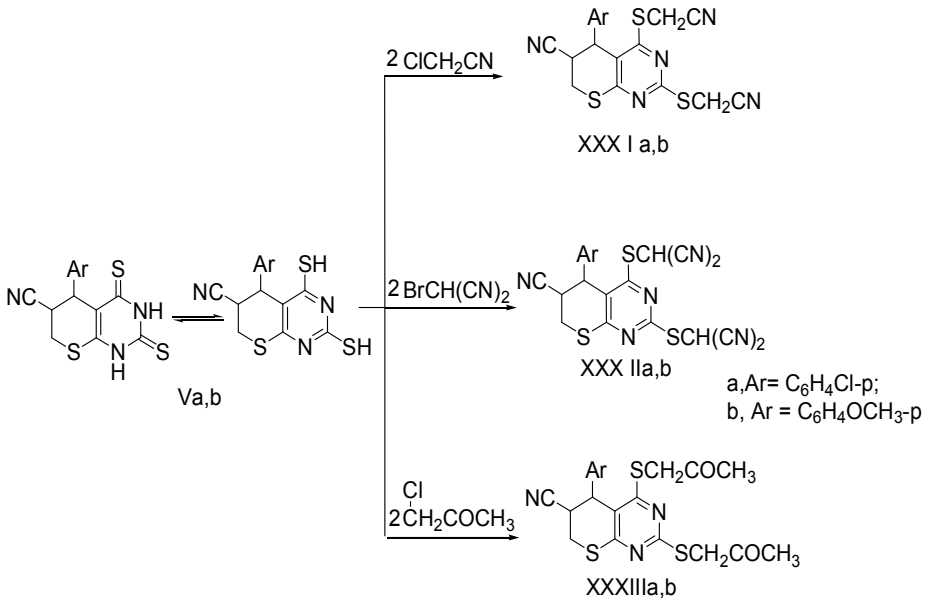
Scheme 11

12- Compounds **Va, b** reacted with a variety of α-halo compounds, namely methyliodide , chloroacetonitrle, monobromo malonitrile, chloroacetone, and phenacylbromide in ethanol in presence of anhydrous potassium carbonate to give S-alkylated compounds. (Scheme 12).



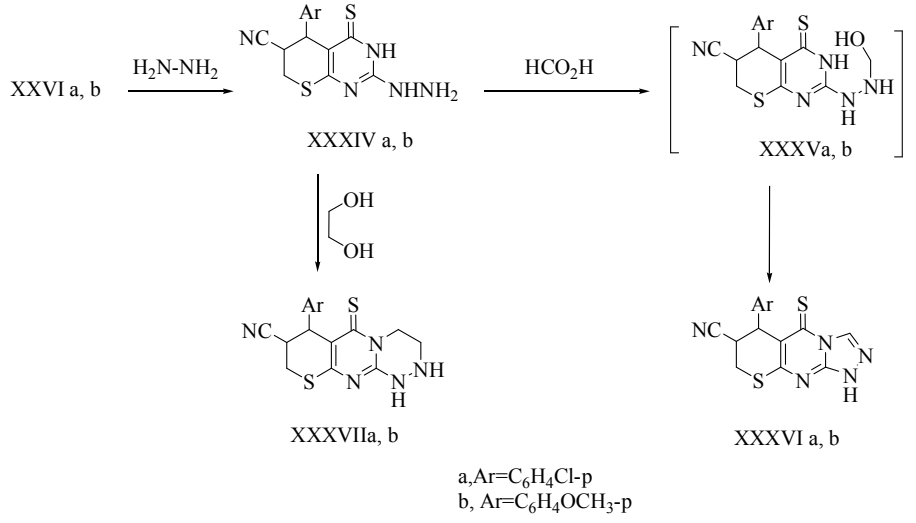
Scheme 12

13-Compounds **Va,b** reacted with two moles of alkyl halides in refluxing sodium ethoxide solution wereby, the*S*,*S*-dialkyl derivatives **XXXI a, b-XXXIIIa,b** were obtained (Sheme 13).



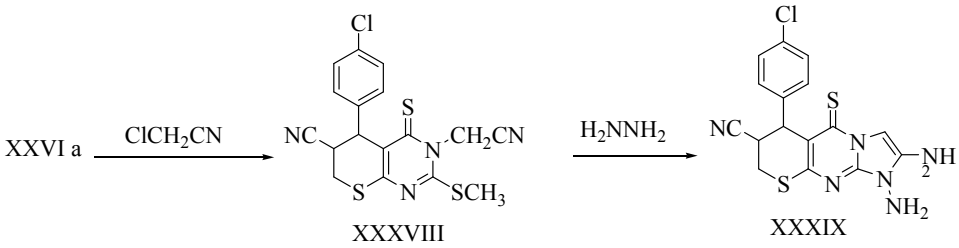
Scheme 13

14-Compounds **XXVI a,b** reacted with hydrazine hydrate in dioxain to give **XXXIV a,b**wich reacted with formic acid and ethylene glycolaccording to scheme 14.



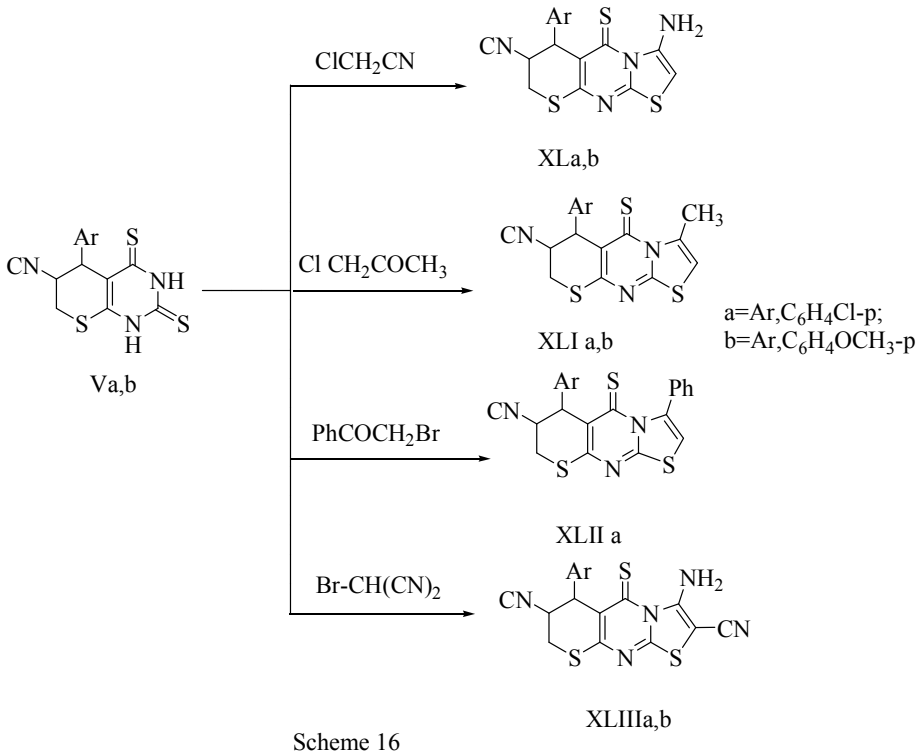
Scheme 14

15- Compound **XXVIa,b** reacted with Chloroacetonitrile to give XXXVIII, the latter reacted with hydrazine hydrate to yield compound **XXXIX** Scheme 15.



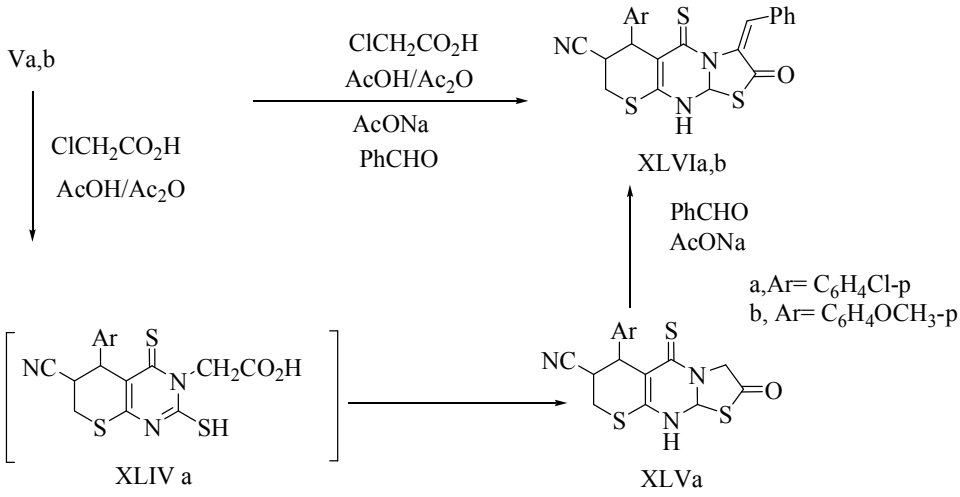
Scheme 15

16- Reaction of α- halocompound **,** namely , chlorocaetonitrile, chloroacetone, phenacylbromide , and mono bromomalononitrile with compound **Va,b** in the presences of sodium ethoxide solution gave cyclic products XL-XLIII(scheme 16).



Scheme 16

17- Reaction of compound **Va,b** with mixture of chloroacetic acid and Benzaldehyde in one-pot reaction in the presences of aceticacid, acetic anhydride and sodium acetate to give compounds **XLVI a,b.**Reaction of compound Va,b with mixture of chloroacetic acid in acetic acid and acetic anhydrideaffered intermediate XLIV. This compound under cyclization gave**XLV**. When **XLV** reacted withbenzaldyde in acetic acid , acetic anhydrideand sodium acetate to give compounds **XLVI a,b.**



Scheme 17

Biological activities

Most of new compounds were evaluated for their antimicrobial properties. Compound II a Showed inhibition zones and therefore antibacterial activity against Staphylococcus aureus (G^+) moderate to the references compound Tetracycline antibacterial agent.

Compound **IIa** showed moderate antibacterial activity against Escherichia coli (G^-) when compared to the reference. While other compounds showed also moderate antibacterial activity against staphylococcus aureus (G^+) and Escherichia coli (G^-).

We can conclude from the result in the table. But there are some compounds show no antibacterials as, **IIb, IIcVb, XVIIb**, **XVa, XXb**, and **XXIIb**. Compound **Va**has antifungal activity, the inhibition zones of **Va**against candida albicans (Fungus) is moderate to the References amphotericin B. While other new compounds showed no antifungal activates against AspergillusFlavus and candida albicans.

Experiment:

This part deals with, the practical procedures used for the synthesis of new compounds, In addition to their physical, spectral and micro-analytical data.