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Recent Advances in the Chemistry of Nitriles and Enaminonitriles

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Abstract

Recent developments in the chemistry of nitriles and enaminonitriles are surveyed with emphasis on the most new findings of our group's work aimed at developing efficient approaches to different heterocyclic compounds as well as correcting some erroneous literature reports and reviews.

Keywords :Active Methylene Nitriles; Arylidenes, Alkylidenes; Dimethylformamide Dimethylacetal; Enaminones; Heterocyclic Compounds.

abbreviations

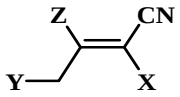
AcOH	Acetic acid
NH_4OAc	Ammonium acetate
NBS	N-Bromo-succinimide
DMAD	Dimethyl acetylene dicarboxylate
DMF	Dimethyl formamide
DMFDMA	Dimethyl formamide dimethyl acetal
EtOH	Ethanol
Pip.	Piperidine
NaOEt	Sodium ethoxide
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
(Bmim)OH	1-Butyl-3-methylimidazolium hydroxide (Ionic Liquid)

1. Introduction

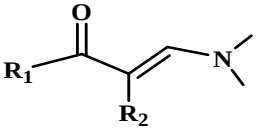
1.1. Synthesis of heterocycles from active nitrile and enaminonitrile intermediates

In the last decades, organic cyano compounds have found extensive utilization in the synthesis of heterocycles. The chemistry of these compounds is very rapidly developing [1] and enormous number of reports, reviews and monographs [2-9] have been recently written to cover the developments in this area. However, due to extensive literature on the subject, none of these articles could afford a complete view of the subject. In the present work, a trial to cover the utility of nitriles and enaminonitriles, especially of the systems **1, 2** and **3** (Figure 1) in the synthesis of different heterocyclic compounds and their fused derivatives will be summarized.

1; X=
a, CN
b, COOEt
c, $CONH_2$
d, $CSNH_2$
e, COPh
f , $CONHNH_2$



2; X	**Y**	**Z**
a, CN	**CN**	**NH_2**
b, COOEt	**COOEt**	**NH_2**
c, CN	**COOEt**	**NH_2**
d, COOEt	**CN**	**NH_2**
e, CN	**SCN**	**Ph**
f, COOEt	**SCN**	**Ph**
g, CN	**COOEt**	**Ph**
h, CN	**CN**	**Ph**
i , COOEt	**H**	**Ph**
j , CN	**H**	**Ph**
k, COPh	**CN**	**Ph**



3	**R^1**	**R^2**
a, Ph	**H**
b, 2-Furyl	**H**
c, 2-Thienyl	**H**
d, CH_3	**$NHCOCH_3$**
e, CH_3	**CONHPh**

Figure 1

It should be stated here that our intention is not to make an encyclopedic scan of the subject but rather to demonstrate the importance and recent advances of these derivatives in the last decade as intermediates in the synthesis of heterocyclic compounds that could be useful to researchers in this field.

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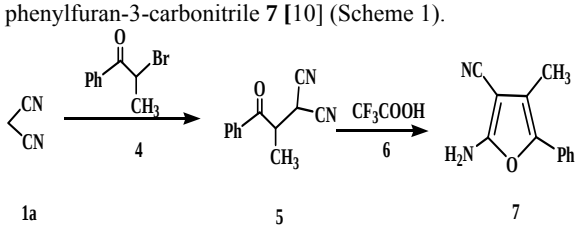
2. Five Membered Rings containing:

2.1. One heteroatom:

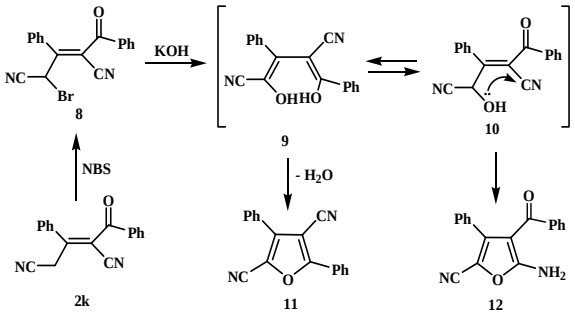
2.1.1. Furan derivatives:

Malononitrile **1a** reacted with 2-bromo-1-phenylpropan-1-one **4** to give 2-(1-methyl-2-oxo-2-phenylethyl) malononitrile **5**, which is cyclized in presence of trifluoro-acetic acid **6** to give 2-amino-4-methyl-5-phenylfuran-3-carbonitrile **7 [**10] (Scheme 1).



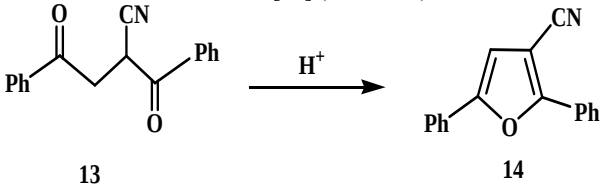
Scheme 1

2-Benzoyl-3-phenylpent-2-enedinitrile 2k underwent bromination with NBS to afford 1-Benzoyl-3-bromo-2-phenylpropenedinitrile derivative 8 [11]. This last compound reacted with potassium hydroxide to afford the furan derivatives 11 and 12 via the intermediates 9 and 10 respectively [12] (Scheme 2).



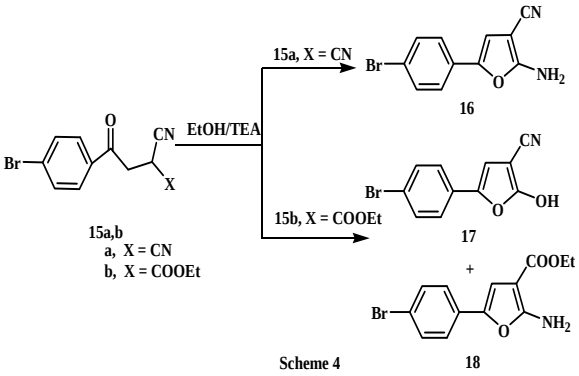
Scheme 2

Under acidic conditions the 1,4-diketone 13 was converted into the furan derivative 14 [13] (Scheme 3).



Scheme 3

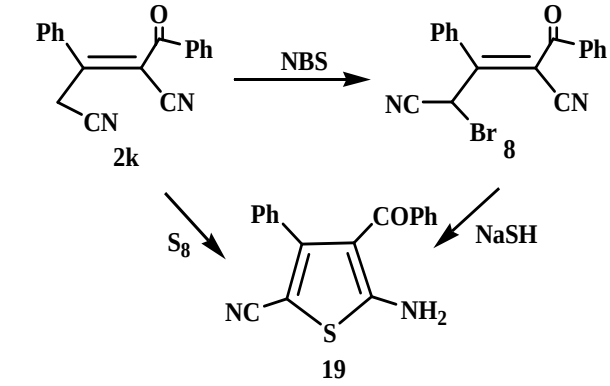
p-Bromo-phenacylnitrile derivatives 15a,b afforded furan derivatives 16, 17 and 18 upon reflux in ethanol catalyzed by triethylamine. 15a afforded 16 as sole product, while 15b afforded a mixture of two furan derivatives 17 and 18 [14](Scheme4).



Scheme 4

2.2. Thiophene Derivatives:

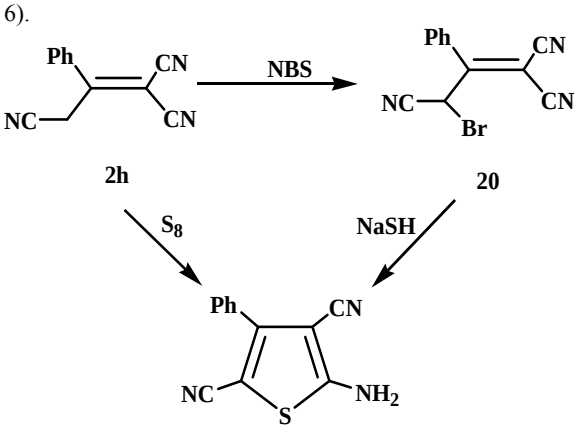
Both 2-benzoyl-3-phenylpent-2-enedinitrile **2k** and 1-Benzoyl-3-bromo-2-phenylpropenedinitrile derivative **8** could be transformed into the thiophene derivative **19** upon the reaction with elemental sulfur or sodium hydrogen sulfide respectively [15] (Scheme 5).



Scheme 5

Compound **2h** is reported to undergo bromination also with NBS to afford the bromo derivative **20**.

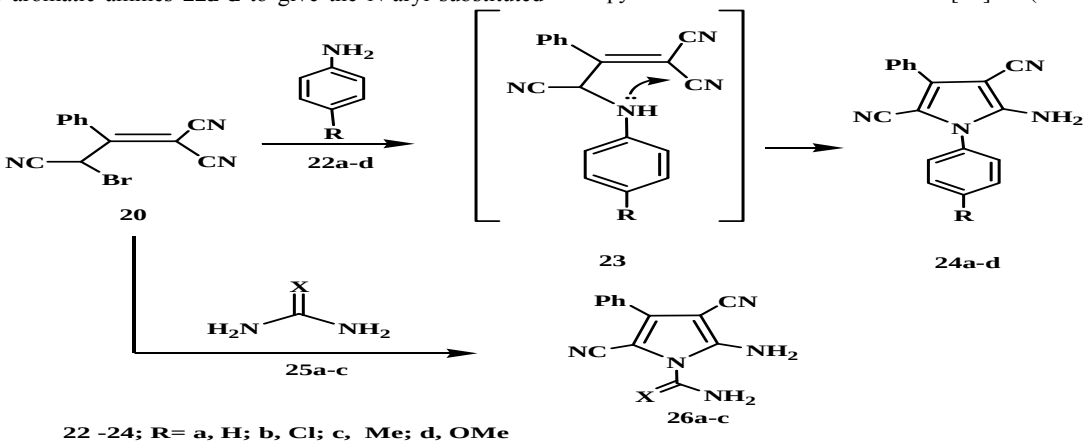
Both **2h** and **20** could be transformed into the thiophene-3,5-dicarbonitrile derivative **21** [16] (Scheme 6).



Scheme 6

2.3. Pyrrole Derivatives:

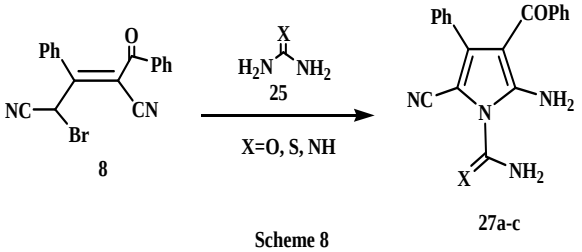
It has been also reported that compound **20** reacts with the aromatic amines **22a-d** to give the N-aryl substituted pyrrole derivatives **24a-d** presumably via the intermediates **23**; and with the urea derivatives **25a-c** to afford the pyrrole derivatives **26a-c** [16] (Scheme 7).



22 -24; R= a, H; b, Cl; c, Me; d, OMe
25, 26; X= a, O; b, S ; c, NH

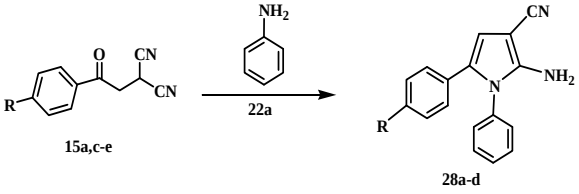
Scheme 7

1-Benzoyl-3-bromo-2-phenylpropenedinitrile derivative **8** is reported to react also with urea, thiourea and guanidine **25a-c** to afford the pyrrole derivatives **27a-c** respectively [15] (Scheme 8).



Scheme 8

The reaction of the phenacylmalononitrile derivatives 15a,c-e with aniline under reflux in absolute ethanol in the presence of catalytic amounts of conc. HCl afforded a single product in each reaction; these compounds were identified as 1,5-disubtituted 2-amino-3-cyano-pyrroles 28a–d [17] (Scheme 9).

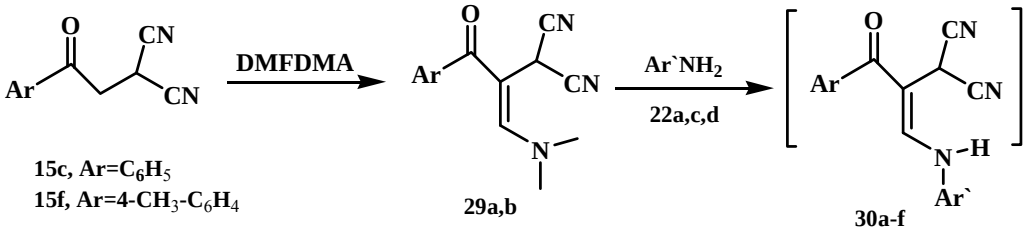


15	R
a	Br
c	H
d	OCH_3
e	F

28	R
a	H
b	Br
c	OCH_3
d	F

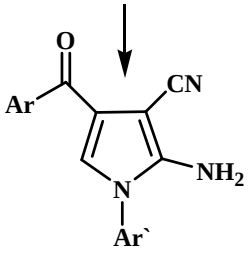
Scheme 9

It has been reported that phenacylmalononitrile derivatives **15c,f** react with dimethylformamide dimethylacetal (DMFDMA) in refluxing toluene to give the enaminones **29a,b** respectively**.** Compounds **29a,b** react with the aromatic amines **22a,c,d** in refluxing ethanol to afford the pyrrole derivatives **31a-f** via the intermediates 3**0a-f** [18] (Scheme 10).



15c, Ar=C_6H_5
15f, Ar=4-CH_3-C_6H_4

31	Ar	Ar`
a	C_6H_5	C_6H_5
b	4-$CH_3C_6H_5$	C_6H_5
c	C_6H_5	4-$CH_3C_6H_5$
d	4-CH3C6H5	4-$CH_3C_6H_5$
e	C_6H_5	4-$CH_3OC_6H_5$
f	4-$CH_3C_6H_5$	4-$CH_3OC_6H_5$

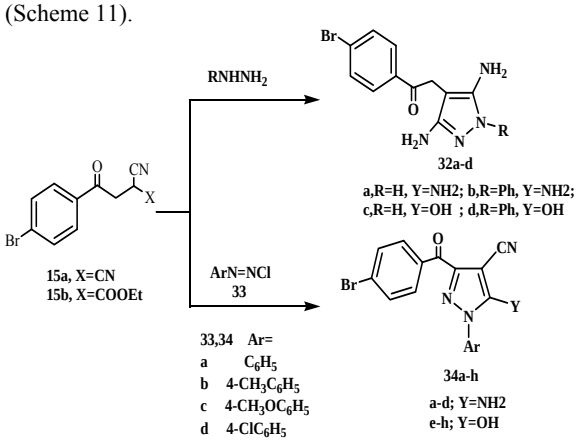


Scheme 10

3. Two Heteroatoms:

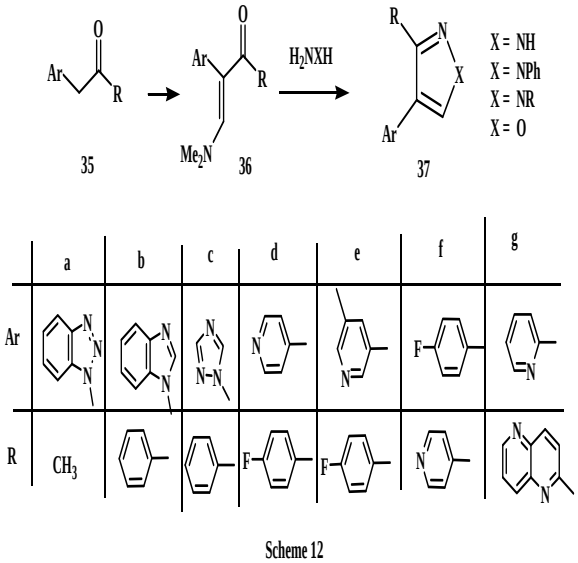
3.1. Pyrazole Derivatives:

P-Bromo-phenacyl malononitrile **15a** reacted with hydrazine derivatives at room temperature to afford the diaminopyrazoles **32a,b** while ethyl *p*-bromo-phenacyl cyanoacetate **15b** afforded the 4-phenacylpyrazole derivatives **32c,d**. Compounds **15a** and **15b** underwent the coupling reaction with the aromatic diazonium salts **33a-d** to afford the pyrazole derivatives **34a-h** respectively [14] (Scheme 11).



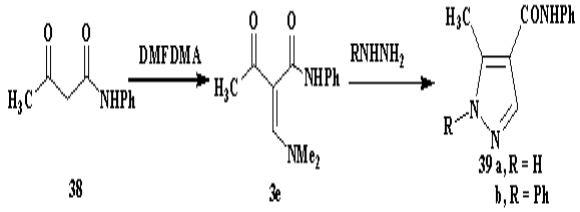
Scheme 11

The carbonyl compounds **35** condensed with DMFDMA to yield the corresponding enaminones **36**. Treatment of the enaminones **36** with hydrazine hydrate, phenyl, or alkyllhydrazines and hydroxylamine afforded the 3,4-disubstituted pyrazoles **37** [19, 20] (Scheme 12).



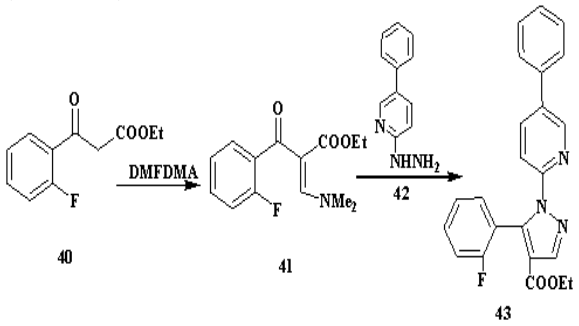
Scheme 12

Acetoacetanilide 38 is reported to react with DMFDMA to afford the enaminone 3e. Treatment of 3e with hydrazine and phenyl hydrazine afforded the respective pyrazole derivatives 39a,b [21-25] (Scheme 13).



Scheme 13

The enaminone 4**1** was obtained from 3-(2-fluoro-phenyl)-3-oxo-propionic acid ethyl ester **40** with DMFDMA and converted directly to the pyrazole derivative **43** by reaction with (5-phenyl-pyridin-2-yl)-hydrazine **42** [26, 27] (Scheme 14).



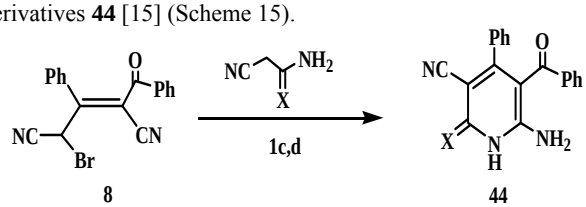
Scheme 14

4. Six Membered Rings Containing:

4.1. One Heteroatom:

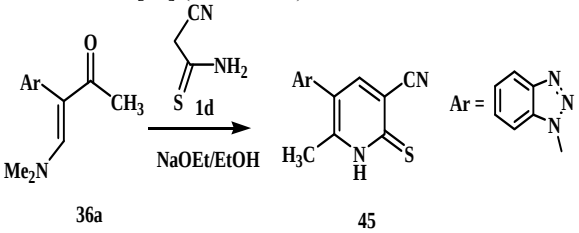
4.1.1. Pyridine Derivatives:

Compound **8** is reported to react with cyanoacetamide **1c** and cyanothioacetamide **1d** to afford the pyridine derivatives **44** [15] (Scheme 15).



Scheme 15

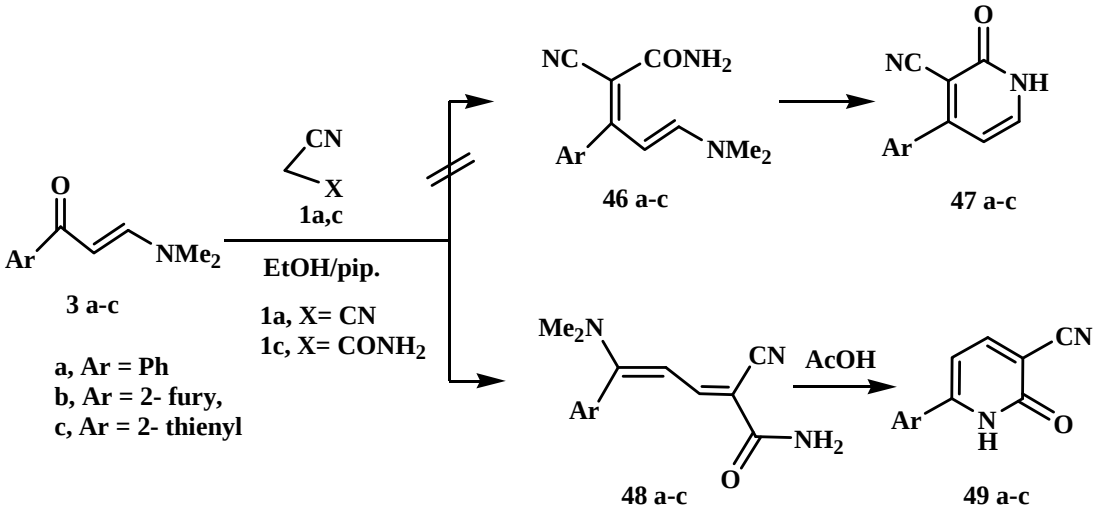
The enaminone 36a reacted with cyanothioacetamide 1d to yield the polyfunctionaly substituted pyridine derivative 45 [27] (Scheme 16).



Scheme 16

The enaminone derivatives **3a-c** are reported to react with malononitrile **1a** to afford the intermediate condensation compounds **46a-c**. These compounds were claimed to undergo cyclization to afford the 2-(1*H*)-pyridone derivatives **47a-c** [28].

However, in a recent reinvestigation of this reaction it has been shown that the intermediates isolated from this reaction are the 2-cyano-5-dimethylamino-5-arylpenta-2,4-dienoic amide derivatives **48a-c** which were cyclized to the 2-(1*H*)-pyridone derivatives **49a-c**, respectively [29] (Scheme 17).



Scheme 17

The structures of the intermediate dienamides **48a-c** were confirmed through X-ray analysis of **48a (**Figure 2**)** and a plausible mechanism for their formation via the intermediate steps **50**-**52** has been suggested [29] (Scheme 18).

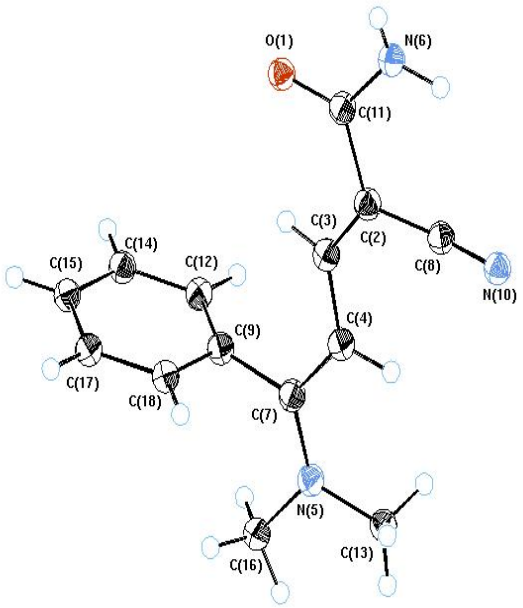
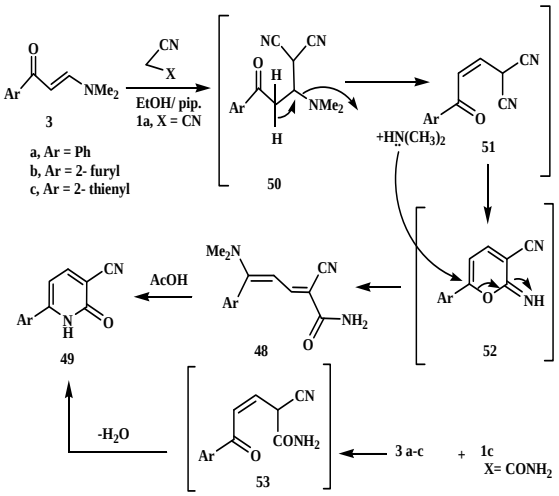


Fig 2: X-ray picture of **48a**.

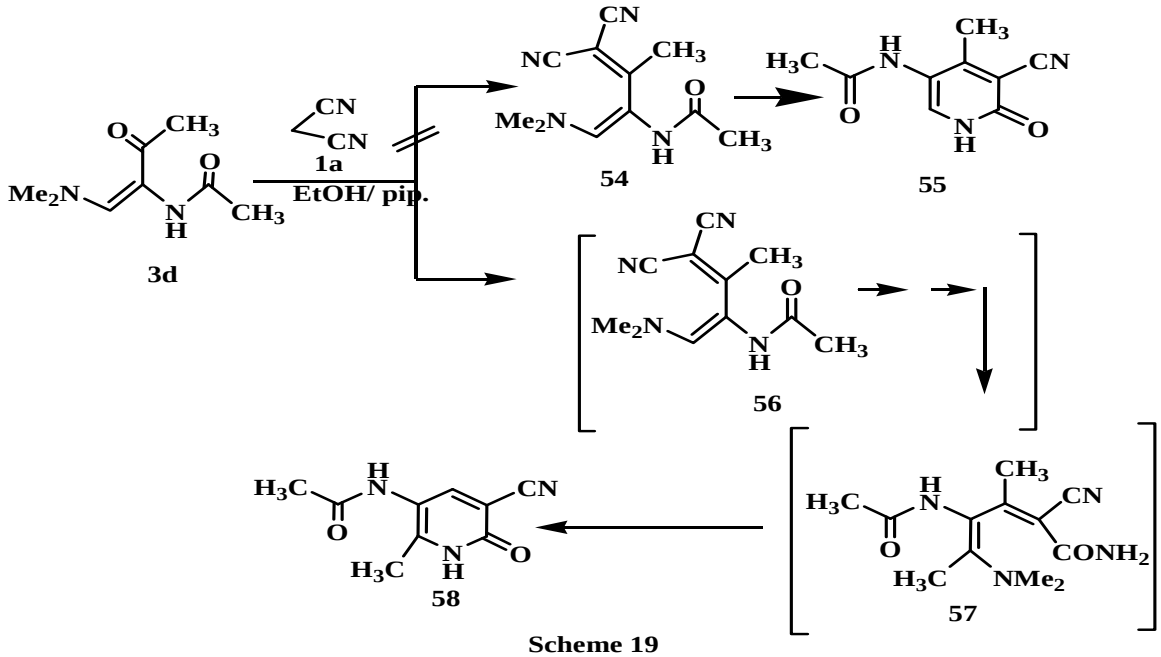


Scheme 18

The reaction of **3a-c** with cyanoacetamide **1c** afforded the same 2-(1*H*)-pyridone **49** presumably via the intermediate **53** which offers a further evidence of the suggested mechanism.

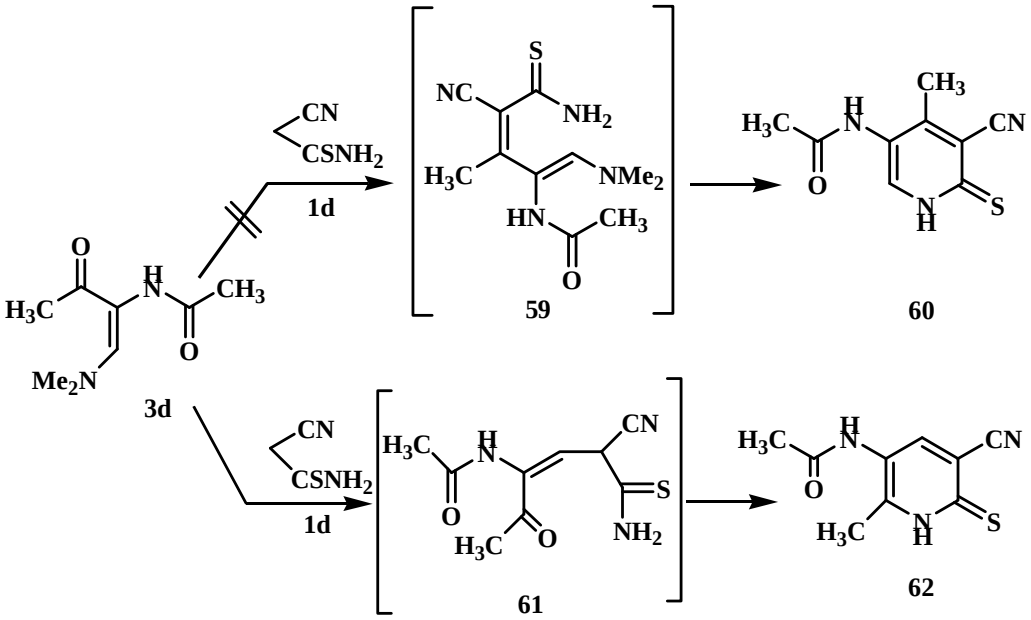
The reaction of 3-acetyl amino-4-dimethylamino-but-3-en-2-one **3d** with malononitrile **1a** was also claimed to afford the condensation intermediate **54** which was claimed to be cyclized to afford 2-(1*H*)-pyridone derivative **55** [30].

Reinvestigation of this reaction showed that it proceeds according to the sequence shown in the previous mechanism to afford the intermediates **56** and **57** which were cyclized into 2-(1*H*)-pyridone derivative **58** [29] (Scheme 19).



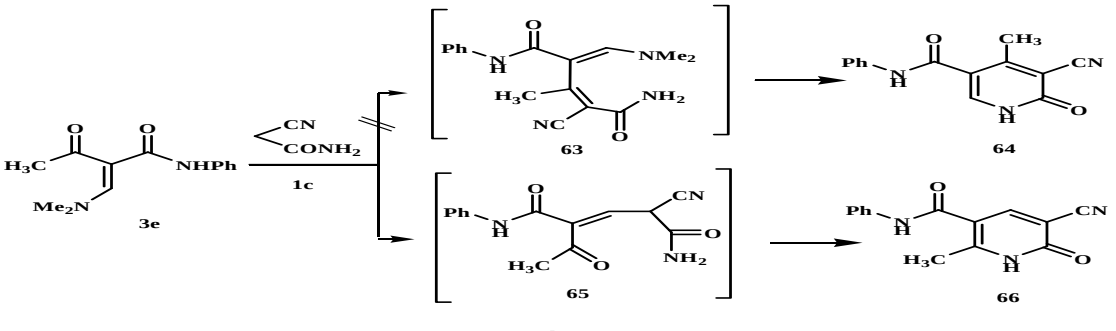
Scheme 19

The reaction of the enaminone **3d** with cyanothioacetamide **1d** was also claimed [30] to afford the 2-(1*H*)-pyridinethione **60** via the condensation intermediate **59.** Reinvestigation of this reaction has also shown that the reaction did not proceed via condensation but rather via substitution of dimethylamino group followed by cyclization of the intermediate **61** to afford **62** [31] (Scheme 20).



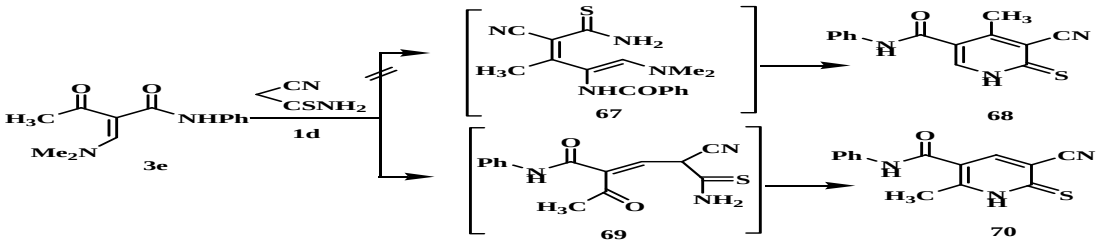
Scheme 20

The reaction of the structurally related compound 2-dimethylaminomethylene-3-oxo-*N*-phenylbutyramide **3e** with cyanoacetamide **1c** was reported to afford the 5-carboamido-3-cyano-4-methylpyridin-2(1*H*)-one derivative **64** assumingly via the condensation intermediate **63** [32, 33]. Reinvestigation of this reaction showed that the 6-methyl 2-(1*H*)-pyridone derivative **66** was obtained presumably via the intermediate **65 [**31] (Scheme 21).



Scheme 21

The reaction of **3e** with cyanothioacetamide **1d** was claimed also to afford the pyridinethione derivative **68** via the condensation intermediate **67** [32]. Reinvestigation of this reaction has also shown that the reaction proceeds via the intermediate **69** followed by cyclization to afford the pyridinethione compound **70** [31] (Scheme 22).



Scheme 22

\Compound 70 was allowed to react with dimethyl acetylene dicarboxylate (DMAD) to afford an addition product via the tautomerized thiol function with loss of the CONHPh group as shown by X-ray crystallography (Figure 3). The X-ray picture shows also that the methyl group is located at the 6th position of the pyridine ring as shown in our structure 70; not in the 4th position as was claimed in structure 68 [32]. \

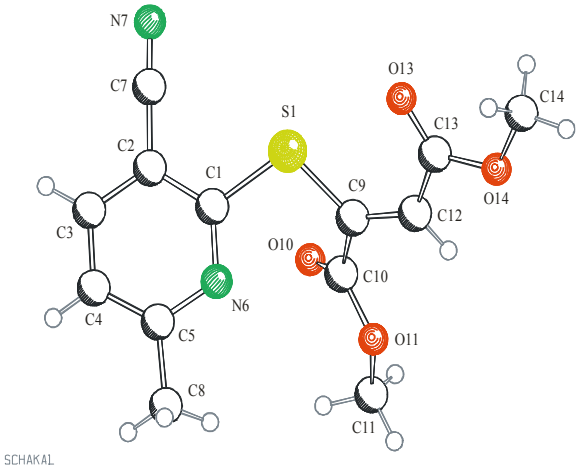
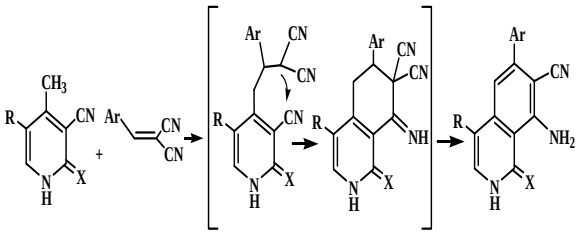


Figure 3: X-ray picture of 70-DMAD adduct

It should be mentioned that the structures of the pyridine-2-(1*H*)-ones **49**, **58**, **66** and pyridine-2-(1*H*)-thiones **62** and **70** are in complete agreement with those reported earlier and confirmed by X-ray study of the products of a related reaction between enaminones and cyanoacetamide **1c** and cyanothioacetamide **1d** [34].

It is worth also to mention here that the position of the aryl group in the erroneous structure **47** and its correct structure **49** seems to be not easily distinguishable by elemental analyses and the spectral data, this is understandable and may seem of little importance to the reader. However it is not understandable and seems of great importance when the substituent becomes a methyl group as in compounds **55** and **60** by Elnagdi et. al. [28, 30] and in compound **64** and **68** by Abu ElMaati et. al.[32, 33]. The authors further claimed that the latter compounds react with the arylidene derivatives of malononitrile to afford the isoquinoline derivatives **71;** and have cited a complete set of analyses and spectra to these imaginary products while initially there is no methyl group in position-4 (Scheme 23).

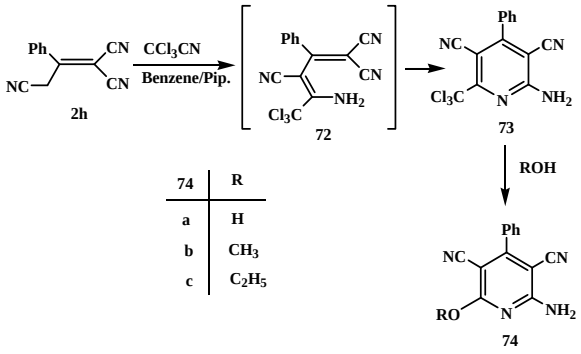


55; R=NHCOCH$_3$, X=O
60; R=NHCOCH$_3$, X=S
64; R=CONHPh, X=O
68; R=CONHPh, X=S

71

Scheme 23

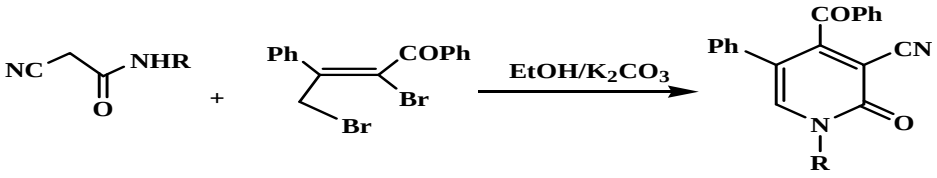
2-Cyanomethylbenzylidine malononitrile **2h** reacts with trichloroacetonitrile in refluxing benzene or toluene catalyzed by piperidine to afford the pyridine **73** presumably via the intermediate **72.** The trichloromethyl moiety in **73** could be easily substituted by OH, OMe, OEt upon refluxing in water, methanol or ethanol, respectively, to afford the pyridine derivatives **74a-c** [35] (Scheme 24).



74	R
a	H
b	CH_3
c	C_2H_5

Scheme 24

We have reported a novel synthesis of the N-substituted pyridone derivatives 76a-f starting from the cyanoacetamide derivatives 1c,f and their related derivatives 1g-j with 1-benzyl-1,3-dibromo-2-phenylpropane 75 in ethanol in presence of potassium carbonate [36] (Scheme 25) .



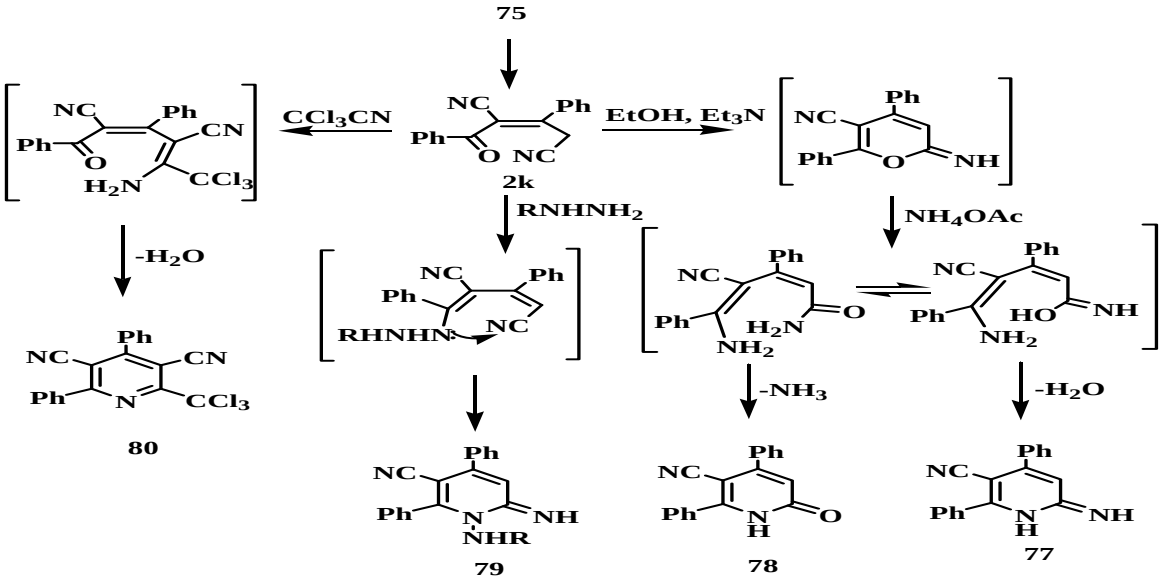
1c, f, g-j **75** **76a-f**

1	R
c	H
f	NH_2
g	N=CHPh
h	Ph
i	4-$CH_3C_6H_4$
j	4-ClC_6H_4

76	R
a	H
b	NH_2
c	N=CHPh
d	Ph
e	4-$CH_3C_6H_4$
f	4-ClC_6H_4

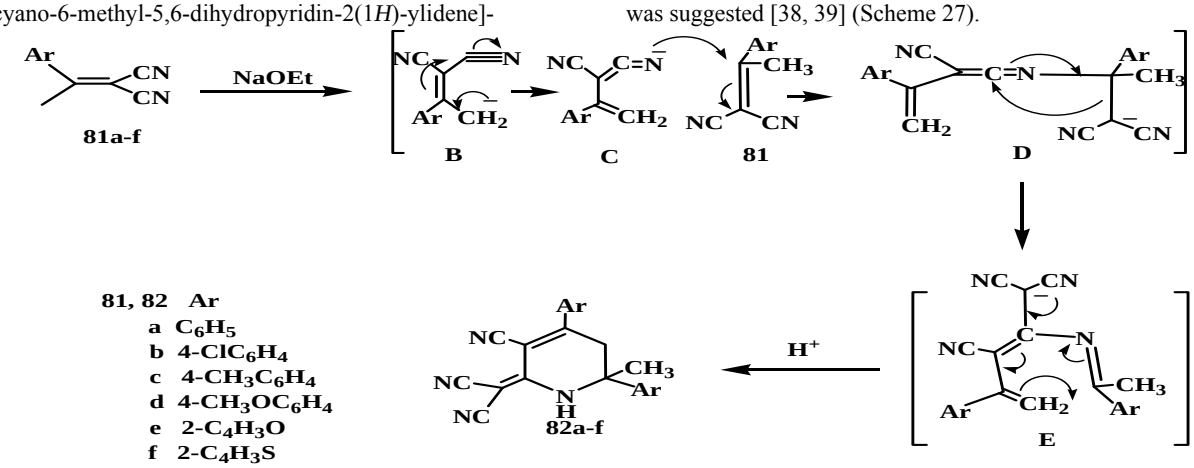
Scheme 25

Compound **75** could be transformed into 2-benzoyl-3-phenylpent-2-enedinitrile **2k**. This last compound could be cyclized with different reagents to afford the new pyridine derivatives **77-80** [37] (Scheme 26)



Scheme 26

Most recently 2-(1-aryl-ethylidene)-malononitriles **81a-f** are reported to undergo self dimerization in ethanol catalyzed by sodium ethoxide to afford 2-[4,6-diaryl-3-cyano-6-methyl-5,6-dihydropyridin-2(1*H*)-ylidene]-malononitrile derivatives **82a-f** respectively. The structure of the dimer was elucidated by X-ray crystallography (Figure 4); and a plausible mechanism for its formation was suggested [38, 39] (Scheme 27).



Scheme 27

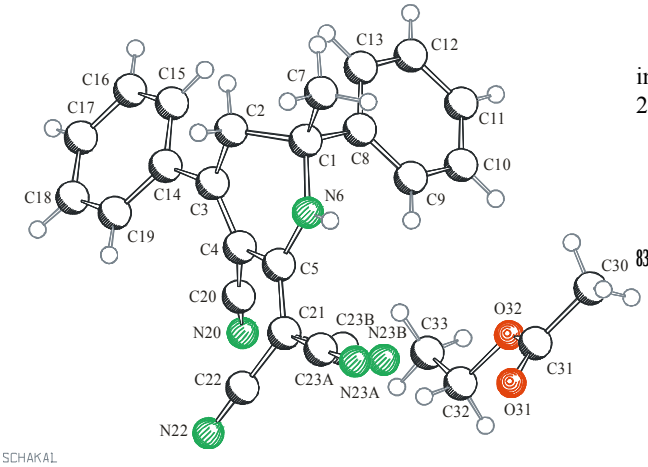
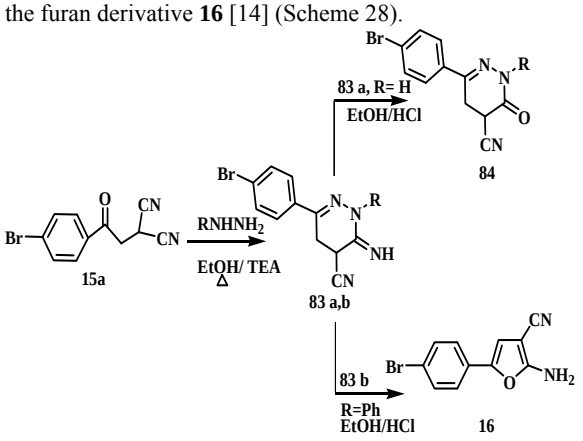


Fig 4.X-ray picture of the dimer **82a.**

4.2. Two Heteroatoms:

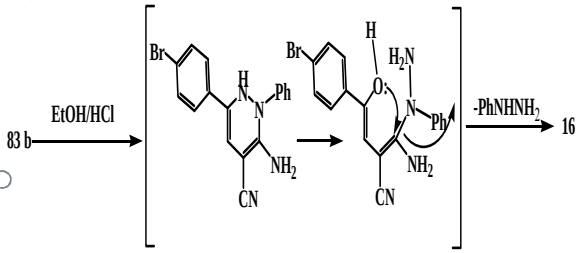
4.2.1. Pyridazine Derivatives:

p-Bromo-phenacyl malononitrile **15a** reacts with hydrazine derivatives in refluxing ethanol catalyzed by triethylamine to afford **83a,b.** Refluxing **83a** in ethanol/hydrochloric acid mixture furnished the pyridazine-6-one **84**. Compound **83b** under the same reaction conditions underwent ring contraction to afford the furan derivative **16** [14] (Scheme 28).



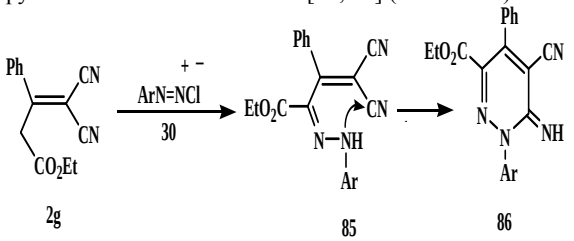
Scheme 28

A plausible mechanism for the transformation of **83b** into the furan derivative **16** was suggested [14] (scheme 29).



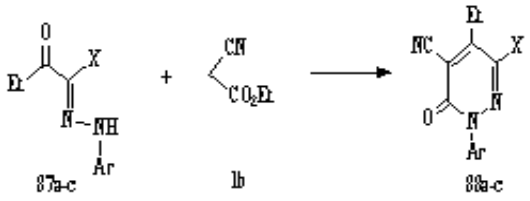
Scheme 29

We have reported that **2g** undergoes the coupling reaction with the aryl diazonium chlorides **30** to yield the hydrazo derivatives **85** which are readily cyclized into the pyridazin-imine derivatives **86** [40, 41] (Scheme 30).



Scheme 30

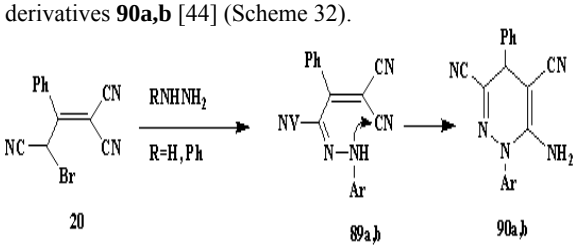
It has also been reported that the arylhydrazones **87a-c** condensed with **1b** to yield the pyridazinones **88a-c** [42, 43] (Scheme 31).



87, 88 a, X=CO2Me; b, X=CN; c, X=CO2Et

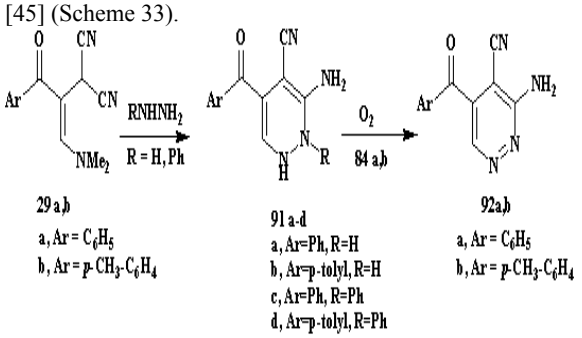
Scheme31

The bromo derivative **20** reacts with hydrazines to afford **89a,b** which could be cyclized into the pyridazine derivatives **90a,b** [44] (Scheme 32).



Scheme 32

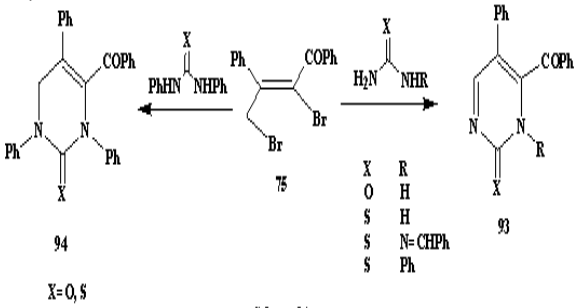
Enaminones **29a,b** (in scheme 10) have been successfully transformed into the pyridazine derivatives **91a-d** through their reaction with hydrazine and phenylhydrazine. The dihydro derivatives **91a,b** could be oxidized to the fully aromatic pyridazine derivatives **92a,b** [45] (Scheme 33).



Scheme 33

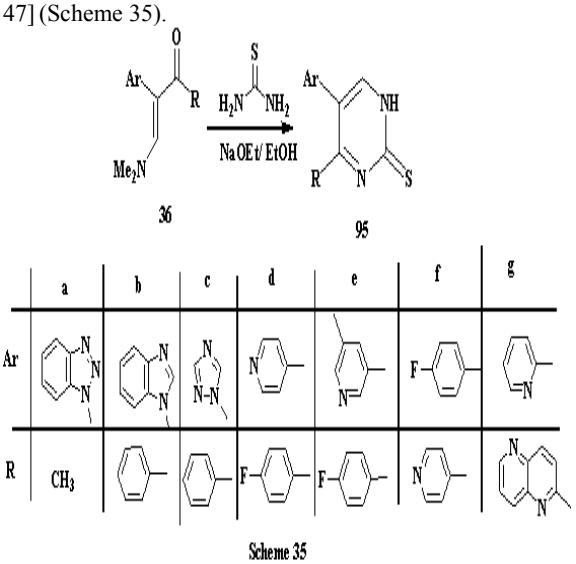
4.2.2. Pyrimidine Derivatives:

Compound **75** is reported to afford the pyrimidine derivatives **93** and **94** upon reaction with mono and disubstituted urea and thiourea derivatives [36] (Scheme 34).



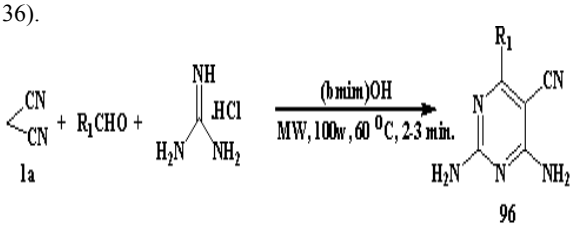
Scheme 34

Treatment of the enaminones **36** with thiourea in the presence of sodium ethoxide afforded the corresponding 4,5-disubstituted pyrimidine-2-thione derivatives **95** [46, 47] (Scheme 35).



Scheme 35

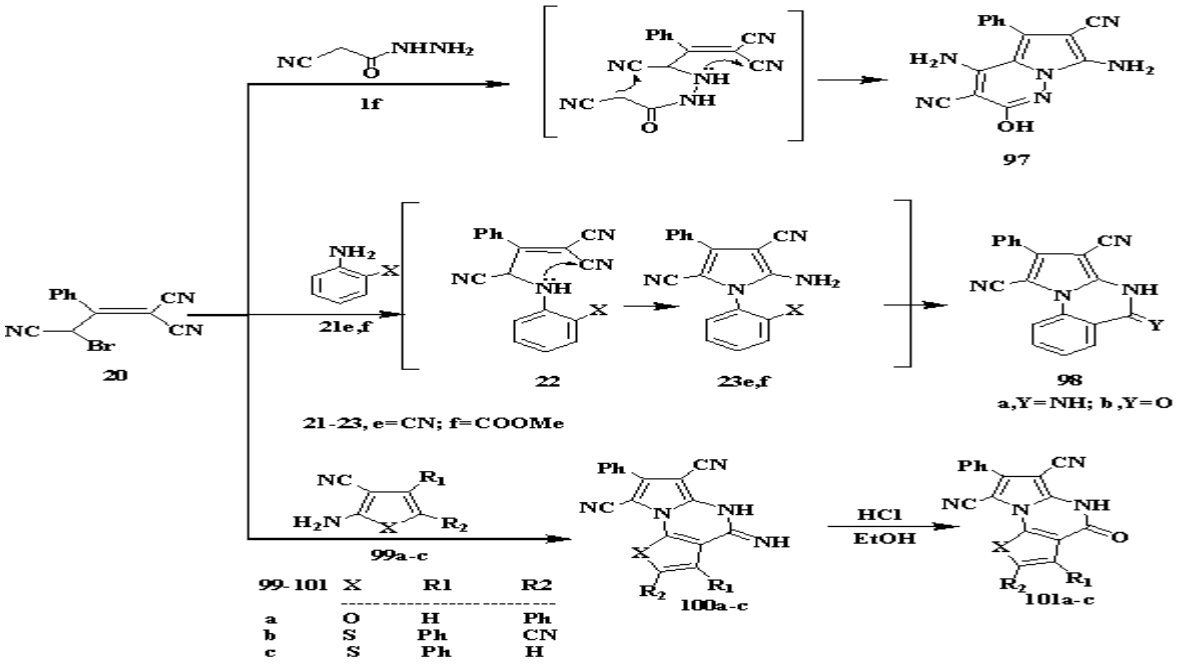
Most recently it has been reported that malononitrile **1a** reacts with different aldehydes and guanidine hydrochloride in a one pot synthesis assisted by microwave in an ionic liquid to afford the pyrimidine derivatives **96** in good to excellent yields [48] (Scheme 36).



Scheme 36

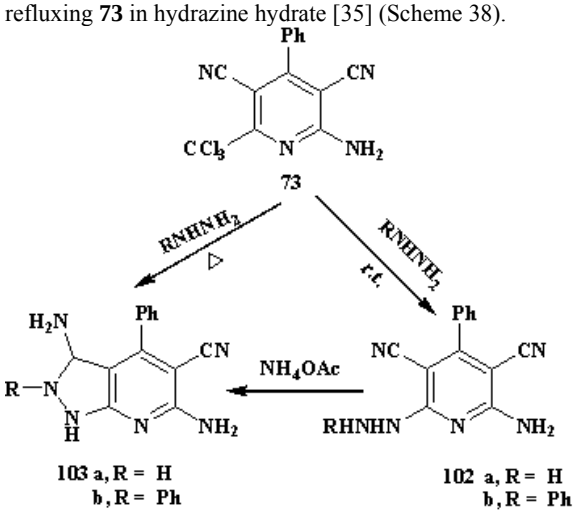
4.2.3. Fused Heterocyclic Rings:

The bromo derivative **20** has been reported to react with cyanoacetohydrazide **1f** to afford the pyrrolo-pyridazine derivative **97**. Compound 20 is also reported to react with anthranilonitrile and methyl anthranilate to afford the pyrroloquinazoline derivatives **98a,b** respectively. It reacts also with the amino furan and thiophene derivatives **99a-c** to afford the imino-indacene derivatives **100a-c** which could be transformed into their –oxo derivatives **101a-c** respectively [16] (Scheme 37).



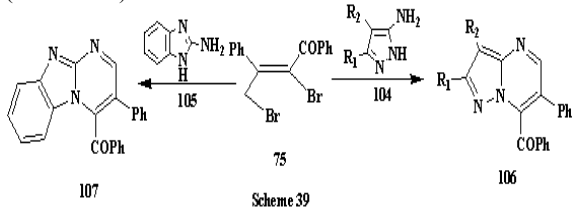
Scheme 37

The trichloromethyl group in compound **73** could be substituted by a hydrazino group upon reaction with hydrazine hydrate at room temperature to afford the pyridyl hydrazine derivatives **102a,b**. Refluxing compounds **102** in ethanol with ammonium acetate afforded the pyrazolo[3,4-b]pyridine derivatives **103a,b**. It worth to mention that **103a,b** were obtained directly upon refluxing **73** in hydrazine hydrate [35] (Scheme 38).



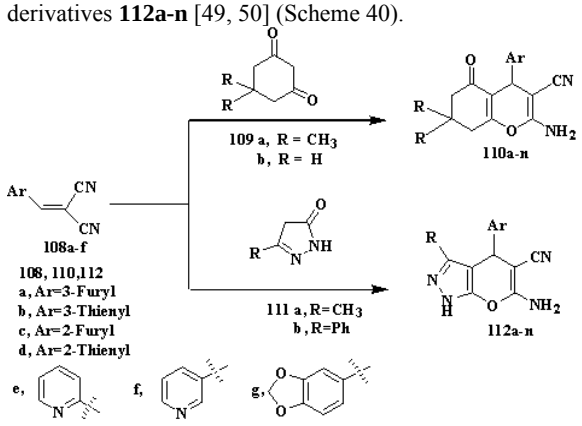
Scheme 38

The dibromo derivative **75** was reported to react with amino pyrazoles **104** and benzimidazole **105** to afford the pyrazolopyrimidine derivatives **106** and the benzimidazolopyrimidine derivative **107** respectively [36] (Scheme 39).



Scheme 39

We have reported that cinnamonitriles derivatives **108a-f** react with the cyclic-1,3-diones **109a**,**b** to afford the novel chromene derivatives **110a-n** and with the NH-pyrazolones **111a,b** to afford the pyranopyrazole derivatives **112a-n** [49, 50] (Scheme 40).



Scheme 40

The structure of these chromene derivatives was unambiguously elucidated via an x-ray crystallographic picture of the formimidate derivative of **110a** (Figure 5) [51].

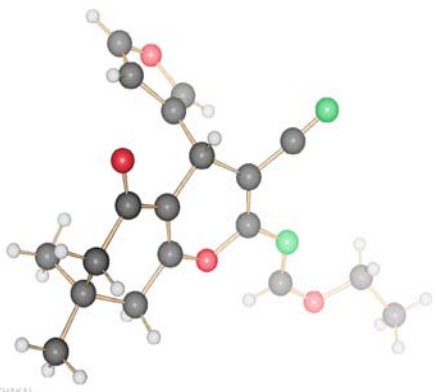
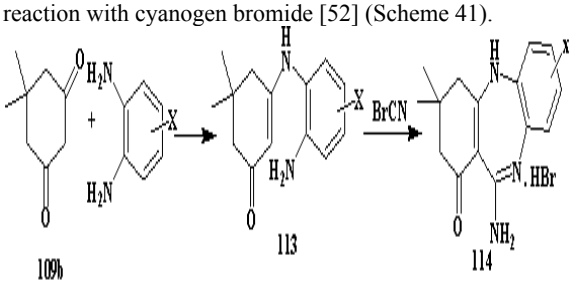


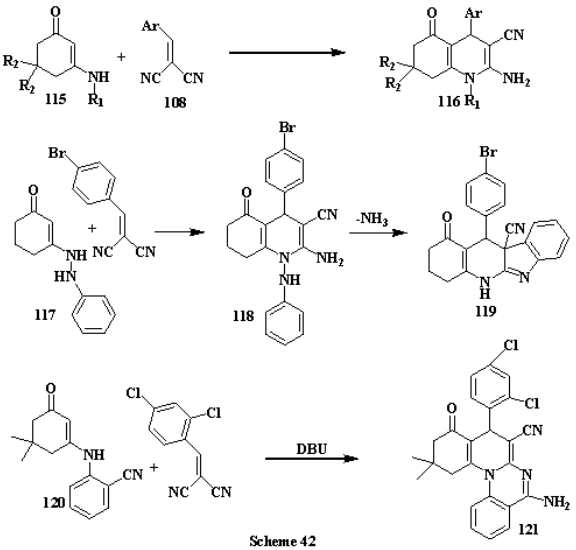
Fig 5. X-ray picture of the formimidate of **110a**

Dimedone **109b** has been reported to react with *o*-phenylenediamines to afford the imine **113** which was cyclized into the benzodiazepine derivatives **114** on reaction with cyanogen bromide [52] (Scheme 41).



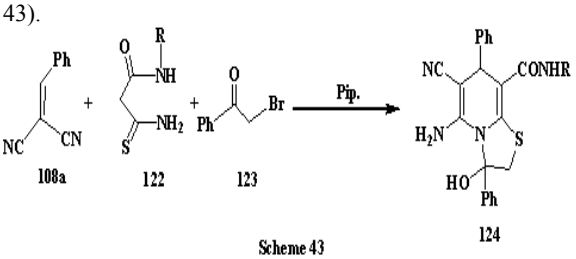
Scheme 41

The cyclic enaminoketones **115** was reported to react with benzylidenes of malononitrile **108** to afford the quinoline derivatives **116**. When a similar reaction was carried out between **117** and *p*-bromo-benzylidene malononitrile the N-anilino-quinoline derivative **118** was obtained which could be cyclized into the indolo-quinoline derivative **119**. Reacting the cyclic enamino-ketone **120** with 2,4-dichloro-benzylidene malononitrile afforded the quinolino-quinazoline **121** [53] (Scheme 42).



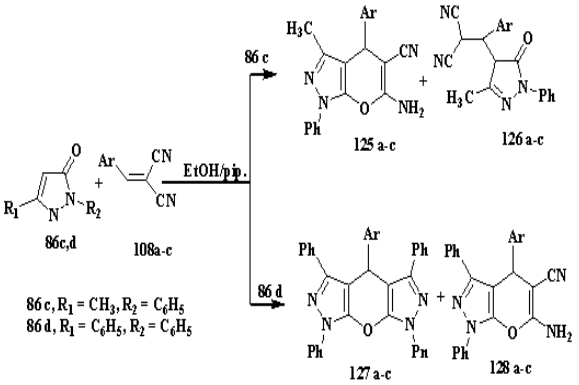
Scheme 42

Benzylidene malononitrile **108a** was reported to react with N-alkyl-2-thicarbamoylacetamide **122** and ω-bromoacetophenone **123** in presence of piperidine to afford the thiazolopyridine derivative **124** [54] (Scheme 43).



Scheme 43

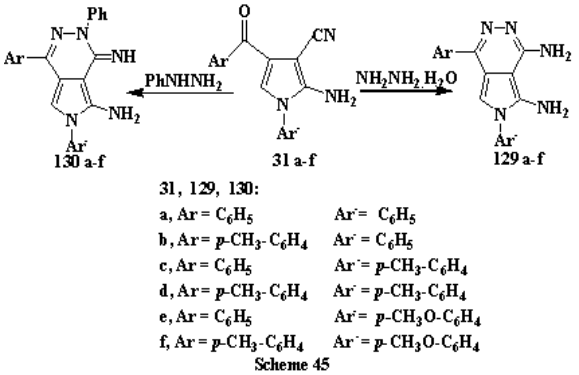
On refluxing different pyrazolone derivatives **86c** with arylidene malononitriles **108a-c** in ethanol catalyzed by piperidine, the pyrano[2,3-c]pyrazolones **125a-c** and the acyclic derivatives **126a-c** were obtained. On the other hand, 1,3-disubstituted pyrazolin-5-one **86d** afforded the oxinobisprazole derivatives **127a-c** and pyrano[2,3-c]pyrazole derivatives **128a-c** [55] (Scheme 44).



Scheme 44

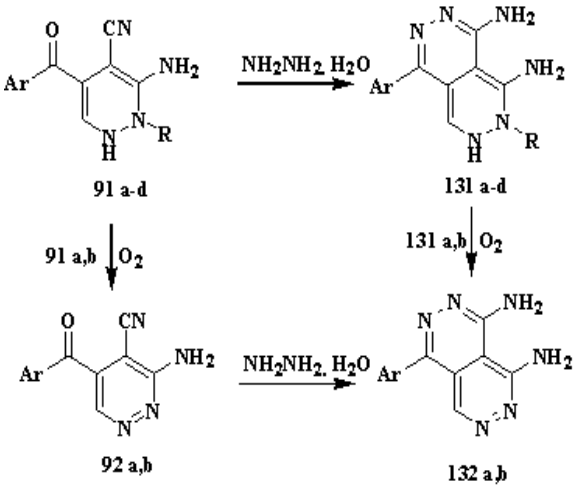
The different behavior of the differently substituted pyrazoline derivatives **86** towards arylidene malononitrile derivatives is rationalized and an interesting mechanism is given in ref. [55].

It has been reported that the pyrrole derivatives **31a-f** react with hydrazine hydrate and phenyl hydrazine in refluxing ethanol to afford the pyrrolo[3,4-*d*]pyridazine derivatives **129a-f** and **130a-f,** respectively [17] (Scheme 45).



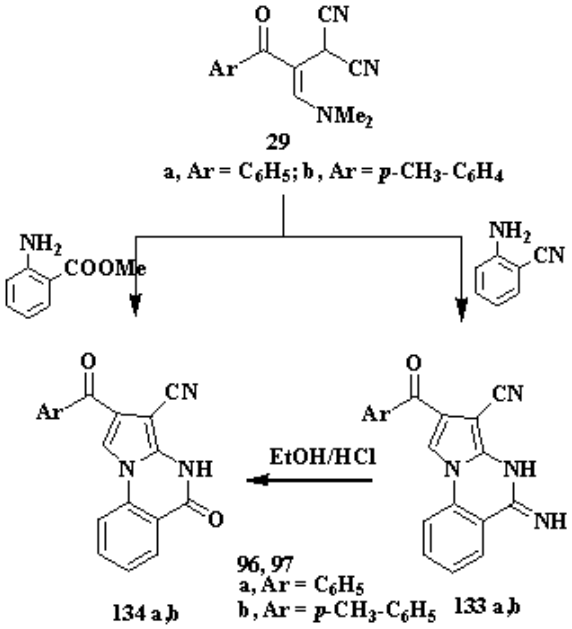
Scheme 45

The pyridazine derivatives **91a-d** and **92a,b** could be transformed into the pyridazino-pyridazine derivatives **131a-d** and **132a,b** respectively [45] (Scheme 46).



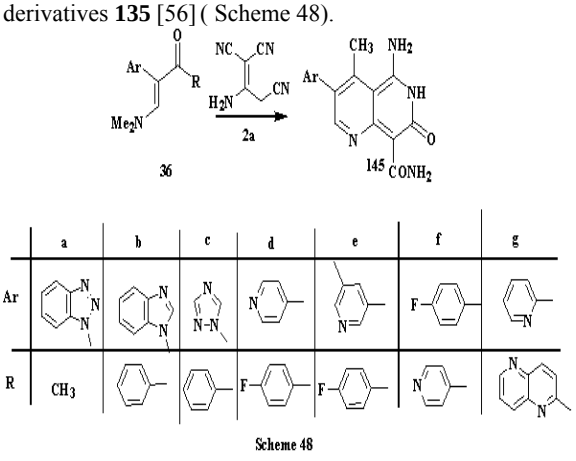
Scheme 46

The enaminones **29a,b** react with anthranilonitrile and methyl anthranilate in refluxing ethanol to afford the 5-iminopyrrolo[1,2-*a*]quinazolines **133a,b** and the oxo-analogues **134a,b** respectively. Compounds **133a,b** could be transformed into **134a,b** upon refluxing in ethanol and conc. HCl [17] (Scheme 47).



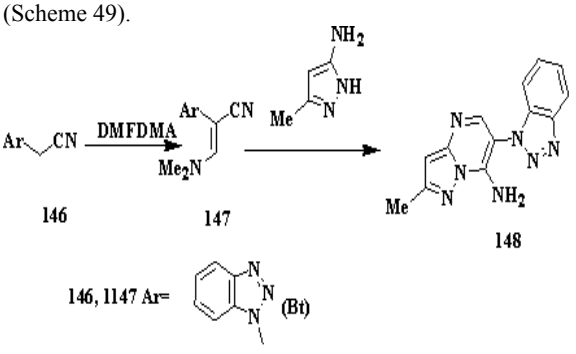
Scheme 47

Treatment of the enaminone derivatives **36** with malononitrile dimmer **2a** afforded 1,6-naphthyridine derivatives **135** [56] (Scheme 48).



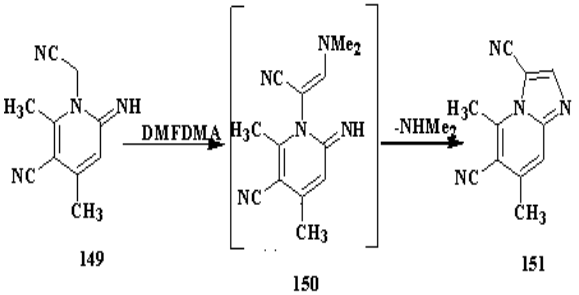
Scheme 48

Benzotriazolyl-acetonitrile **146** condenses with DMFDMA to afford the enaminonitrile derivative **147**. The reaction of **147** with 5-amino-3-methyl pyrazole afforded the pyrazolopyrimidine derivative **148** [57] (Scheme 49).



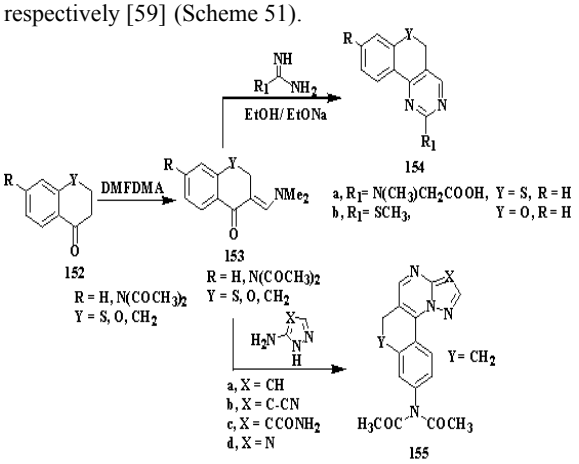
Scheme 49

Imidazo[1,2-*a*]pyridine derivative **151** could be obtained via the reaction of **149** with DMFDMA through the intermediate enamine derivative **150** [58] (Scheme 50).



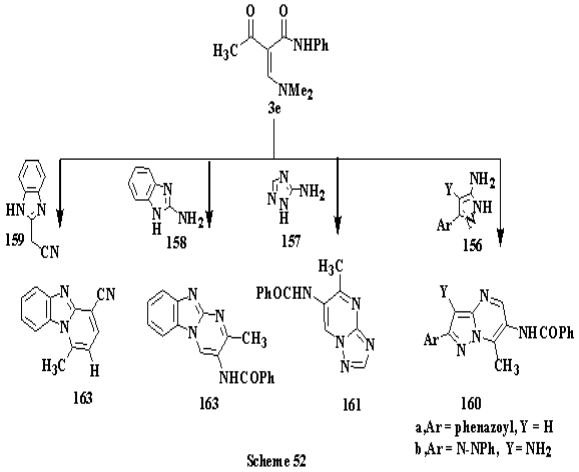
Scheme 50

Refluxing of compounds **152** with DMFDMA provided the enaminones **153**, which were directly allowed to react with bi-nucleophiles such as substituted guanidine and amino azoles (3-aminopyrazoles, 3-amino-1,2,4-triazole) to give the fused ring systems **154a,b** and **155a–d** respectively [59] (Scheme 51).



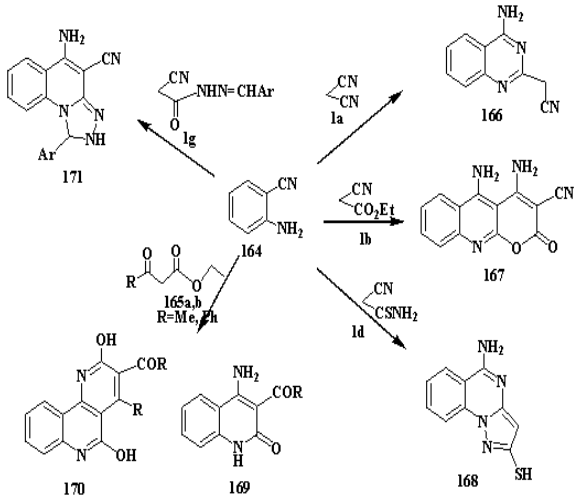
Scheme 51

The enaminone **3e** reacted with pyrazoles **156,** 1,2,4-triazole **157**, 2-aminobenzimidazole **158** and (1*H*-benzimidazol-2-yl)-acetonitrile **159** to produce pyrazolo[1,5-*a*]pyrimidines **160**, triazolo[1,5-*a*]pyrimidine **161**, the pyrimido[1,2-*a*]benzimidazole **162** and 1-methylbenzo[4,5]imidazo[1,2-*a*]pyridine-4-carbonitrile **163** respectively [23] (Scheme 52).



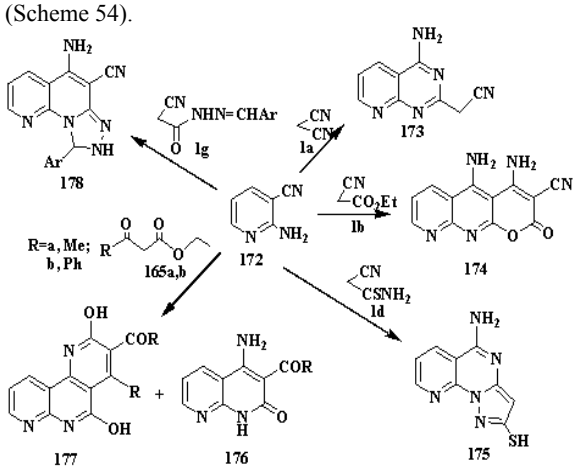
Scheme 52

Anthranilonitrile **164** is reported to react with malononitrile **1a**, ethyl cyanoacetate **1b**, cyanothioacetamide **1d**, β-ketoesters **165a,b**, arylidenes of cyanoacetohydrazide **1g** to afford the fused ring systems **166-171** respectively [60] (Scheme 53).



Scheme 53

2-Aminonicotinonitrile **172** is also reported to react similarly with the above mentioned reagents to afford the fused heterocyclic systems **173-178** respectively [61] (Scheme 54).



Scheme 54

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