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CHEMISTRY OF HYDRAZONOALKANENITRILES

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Abstract – Reactions of arene and heteroaromatics diazonium salts with active methylene compounds having cyano group have been illustrated to afford hydrazonoalkanenitriles with a range of substituents. Structural investigation for hydrazonoalkanenitriles has been made. Furthermore the reactivity of hyrazonoalkanenitriles towards nucleophilic and electrophilic reagents has been displayed.

1. INTRODUCTION

Hydrazonoalkanenitriles with cyano function as electrophilic moiety and hydrazone nitrogen as nucleophilic one are bidentate reagents. They are interesting precursors to a variety of heteroaromatics. The synthetic approaches to hydrazononitriles as well as their chemistry are affected by the relative position of the hydrazone and nitrile functionality. There are several situations, 2-hydrazononitriles **1A**, 3-hydrazononitriles **1B**, and 4-hydrazononitriles **1C**. In compound **1A** the hydrazone and nitrile moieties cannot undergo intramolecular cyclization in contrast to **1B** and **1C** where intramolecular cyclization into heteroaromatic five or six membered ring is very ready and thus only under special condition the acyclic **1B** and **1C** have been made. In the present article reported synthesis of hydrazones **1A-C** will be summarized. Only chemical reactivity of **1A** however will be discussed.

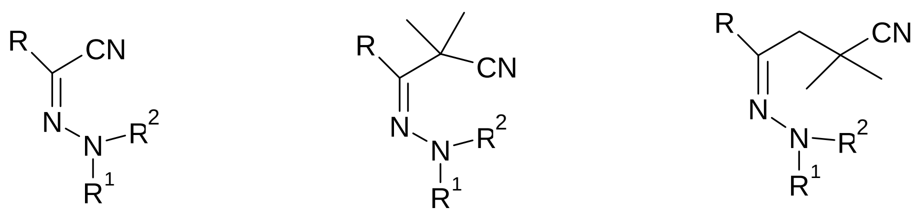
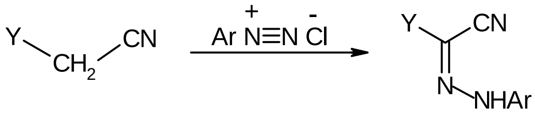

1A **1B** **1C**

Chart 1

2. SYNTHETIC APPROACHES TO HYDRAZONOALKANENITRILES

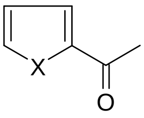
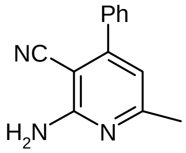
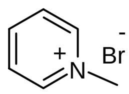
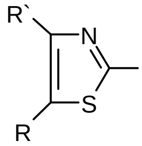
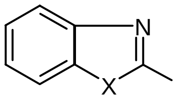
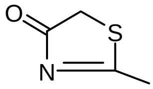
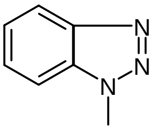
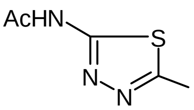
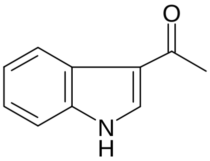
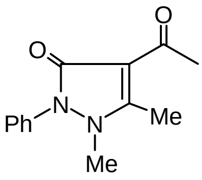
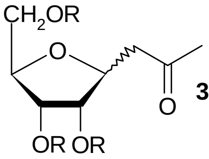
2.1. COUPLING COMPOUNDS HAVING CYANO GROUP WITH AROMATIC DIAZONIUM SALTS

Active methylene nitriles readily couple with aromatic diazonium salts in presence of sodium acetate[1-15] to yield the corresponding arylhydrazonoalkane nitriles (Table 1).

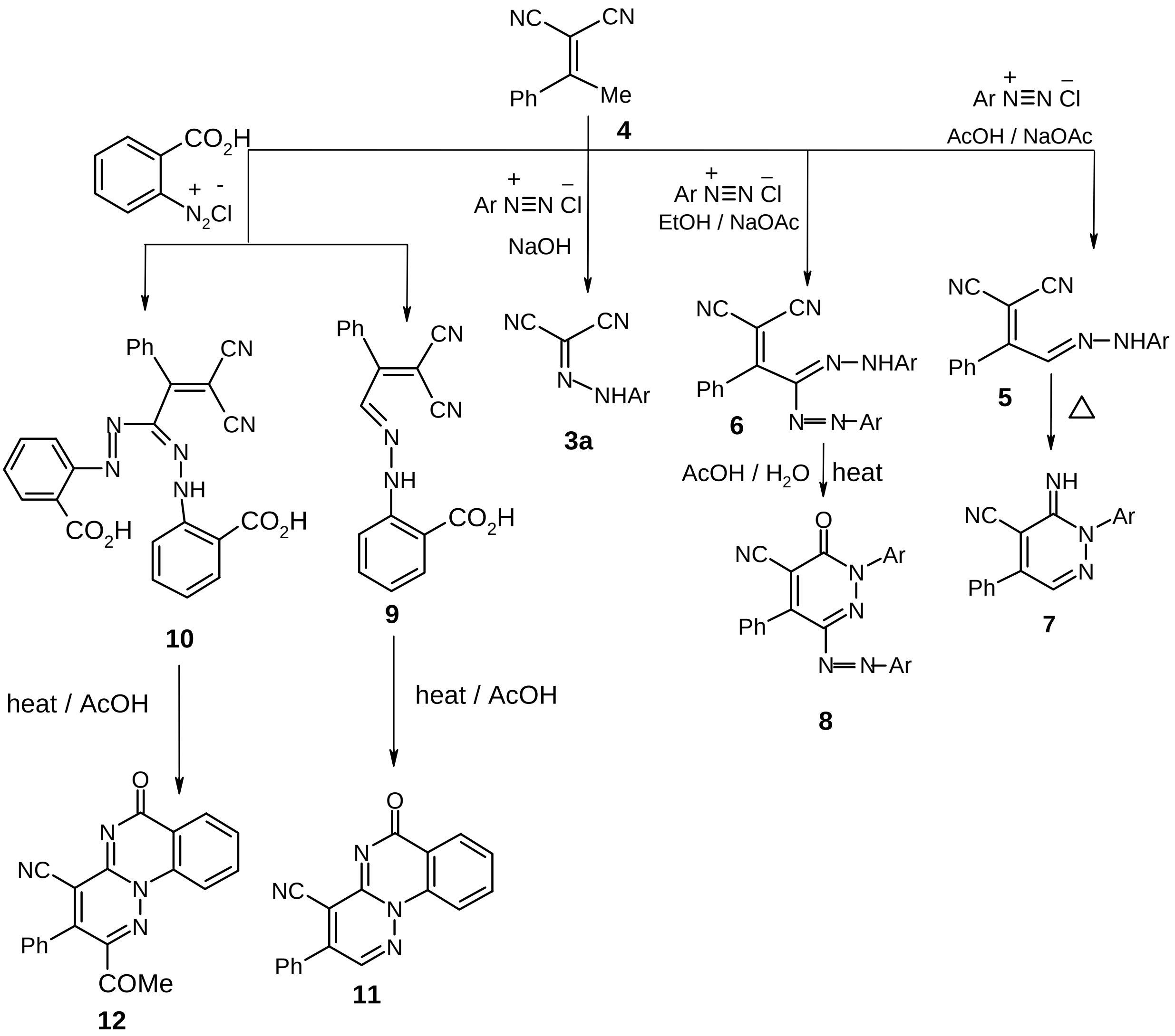


2a-v **3a-v**

Table 1. Coupling of active methylene compounds **2a-v** with aromatic diazonium salts

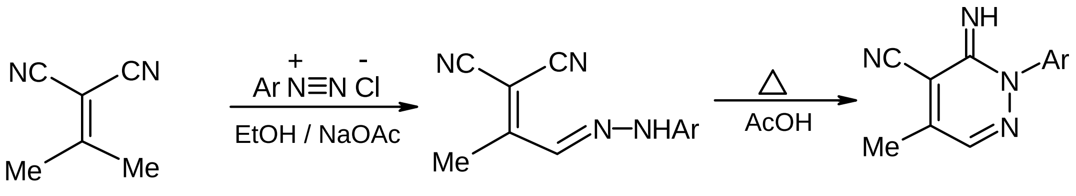
Entry	Y	Compd. No.	Ref.	Entry	Y	Compd. No.	Ref.
1	CN	**3a**	3,16	12	 [X = O, S]	**3l-m**	32
2	CO_2Et	**3b**	3,4,9,17				
3	COR	**3c**	5,7,18,19				
4	$CONH_2$	**3d**	20				
5	$CSNH_2$	**3e**	21	13		**3n**	33
6	$CONHNH_2$	**3f**	22				
7	$4\text{-}NO_2C_6H_4$	**3g**	23	14		**3o**	34
8		**3h**	21,24-29	15	 [X = O, S, NH, NMe]	**3p-s**	35-38
9		**3i**	21,24-29	16		**3t**	38
10		**3j**	30	17		**3u**	146
11		**3k**	31	18		**3v**	39

2-Cyano-3-substituted crotononitriles **4** coupled with aromatic diazonium salts to yield either **5** or **6** depending on the applied reaction condition.[40,41] Compound **5** readily afforded the pyridazinimine **7** while **6** gave the arylazopyridazinone **8** upon cyclization under the stated conditions. It was reported that[42] coupling **4** with benzenediazonium chloride in presence of sodium hydroxide gives **3a.** Also coupling **4** with diazotized anthranilic acid affords the monohydrazone **9** or the amidrazone **10** depending on the applied reaction condition. Whereas **9** cyclized smoothly on refluxing in acetic acid into pyridazino[2,3-*a*] qinazolinone derivative **11**, the amidrazone **10** afforded the acetyl derivative of **12** when treated under the same condition[43] (cf. Scheme 1).



Scheme 1

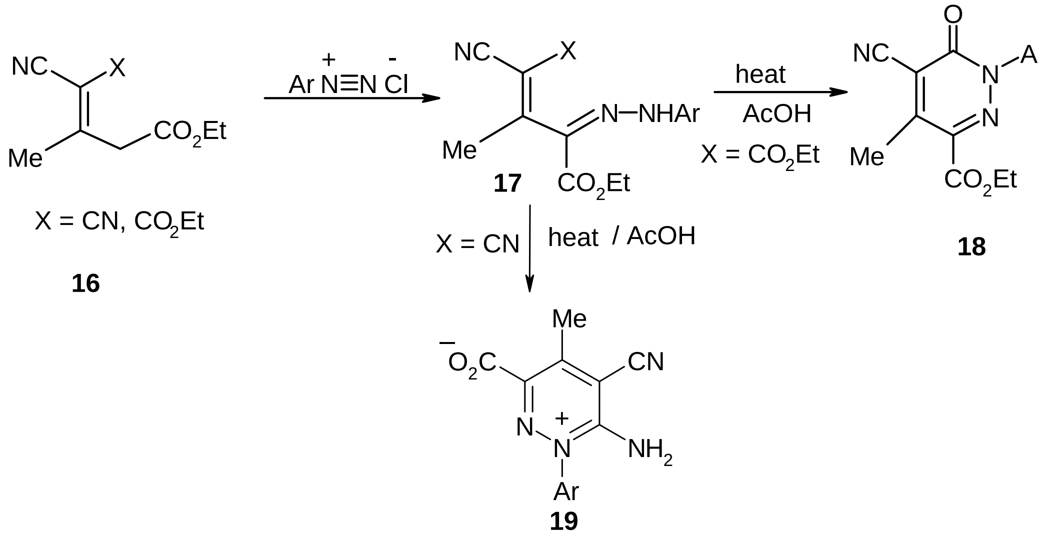
While coupling **13** with aromatic diazonium salts in ethanolic sodium acetate affords the arylhydrazones **14** which could not be isolated in a pure form, the pyridazinimine **15** was isolated on short reflux of the hydrazone in acetic acid[40] (cf. Scheme 2).



13 **14** **15**

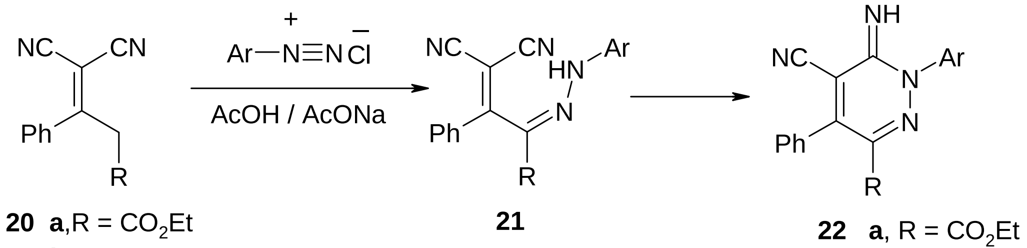
Scheme 2

Also the substituted crotononitrile **16**[40,44,45] couples with the aromatic diazonium salts to afford the acyclic hydrazone **17** which on boiling in acetic acid affords the pyridazinone **18** or pyidazine carboxylate **19** (cf. Scheme 3).



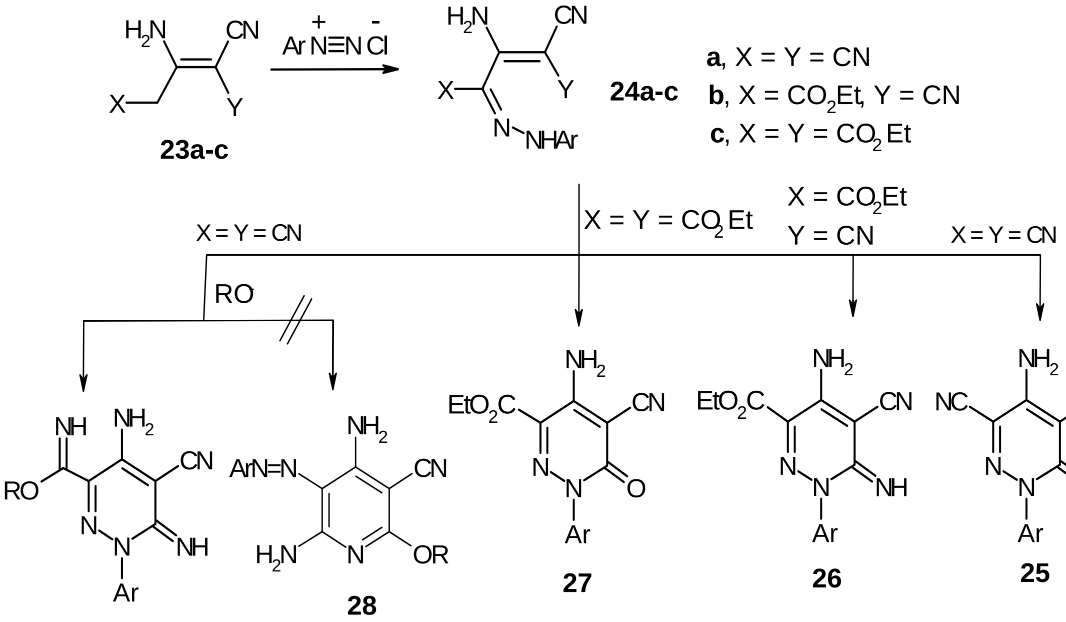
Scheme 3

Other examples are cyclization of products of coupling **20a,b** with aromatic diazonium salts into pyridazinimines **22a,b**[46,47] (cf. Scheme 4).



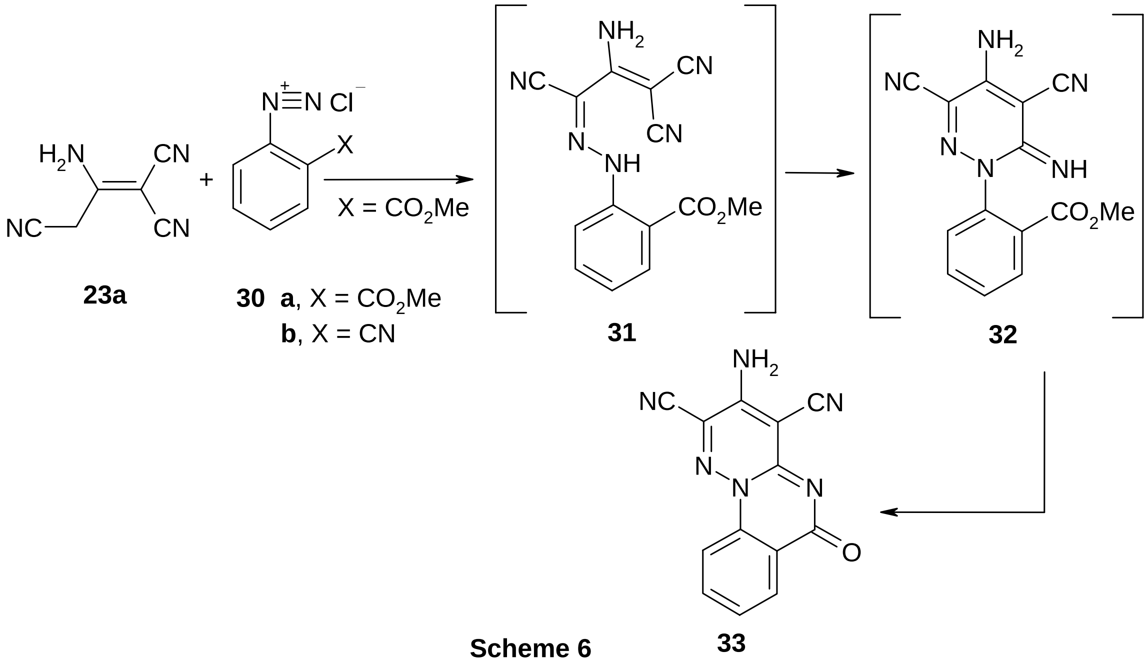
Scheme 4

Aromatic diazonium salts couple with functionally substituted crotononitriles **23a-c** affording the corresponding hydrazones **24a-c**, that cyclized readily into the pyridazinimine **25**, **26** and the pyridazinone **27**.[44,48-59] Mittelbach *et al.*[60] has reported that **24a** as soon as it is formed in the reaction medium cyclized to form **25**. This suggestion was later rejected by Elnagdi *et al.*[49,50] based on ^{13}C NMR data, pK_a values as well as electrochemical behavior of this product that support their believe that the product is really the hydrazone **24a.** Junek[61] has reported that **24a** was cyclized into the pyridine **28** on treatment with alkoxides. Recently Elnagdi *et al.* [62] suggested that **28** is really **29** (cf. Scheme 5).



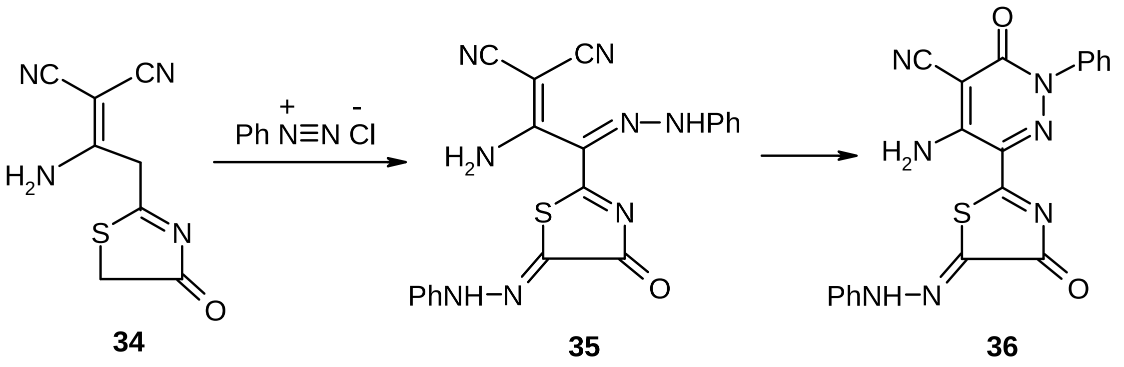
Scheme 5

Diazonium salts of methyl anthranilate **30a** or anthranilonitrile **30b** couples with nitriles **23a** to give hydrazones **31** that simultaneously cyclises into pyridazinimines **32** then to pyridazinoquinazolines **33**.[54] (cf. Scheme 6).



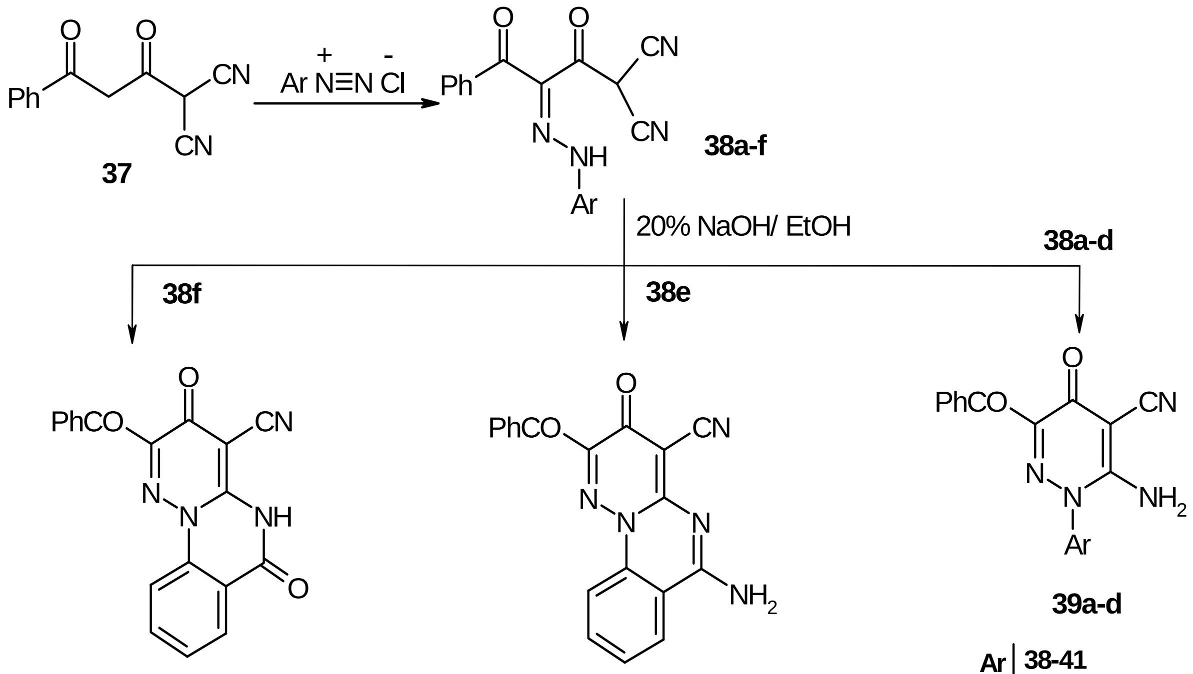
Scheme 6

Recent application of this approach is the coupling of 1-amino-2-(4-oxothiazolin-2-yl)ethylidene-malononitrile **34** with benzenediazonium chloride to yield the corresponding diphenylhydrazone **35** that was cyclized into the thiazolylpyridazinone **36**[63] (cf. Scheme 7).



Scheme 7

2-Cyano-5-phenyl-3,5-dioxopentanonitrile (**37**) undergoes coupling reaction with the aromatic diazonium salts to afford the colored hydrazo products **38a-f**. Refluxing compounds **38a-d** in ethanolic sodium hydroxide accomplished their cyclization to the pyridazine derivatives **39a-d,** while the same treatment of compound **38e** and **38f** led to the pyridazino[2,3-*a*]quinazoline derivatives **40** and **41** respectively[64] (cf. Scheme 8).



41

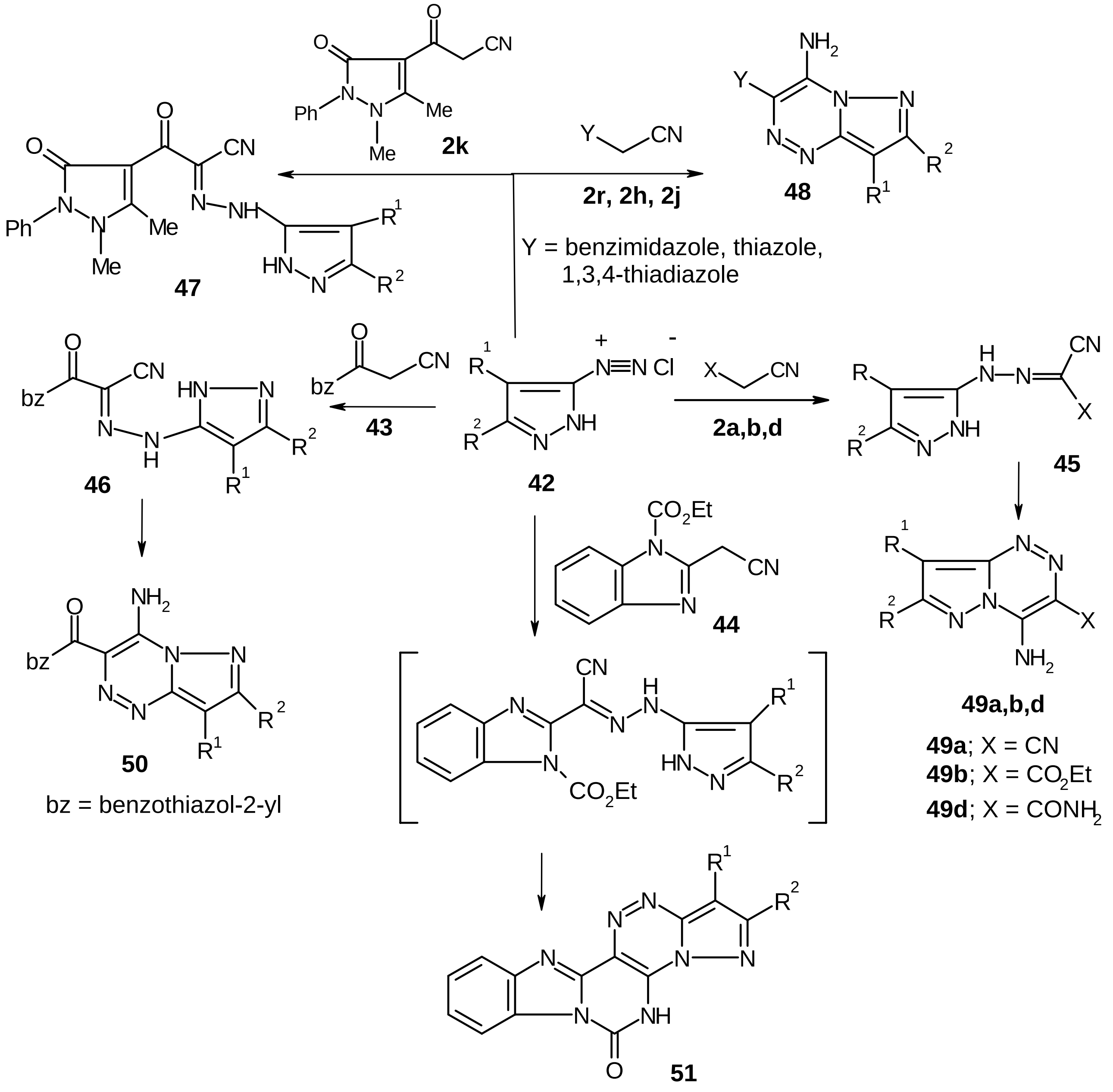
40

Ar	38-41
a	C_6H_5
b	4- $MeOC_6H_4$
c	4- ClC_6H_4
d	4- MeC_6H_4
e	2- NCC_6H_4
f	2- $MeO_2CC_6H_4$

Scheme 8

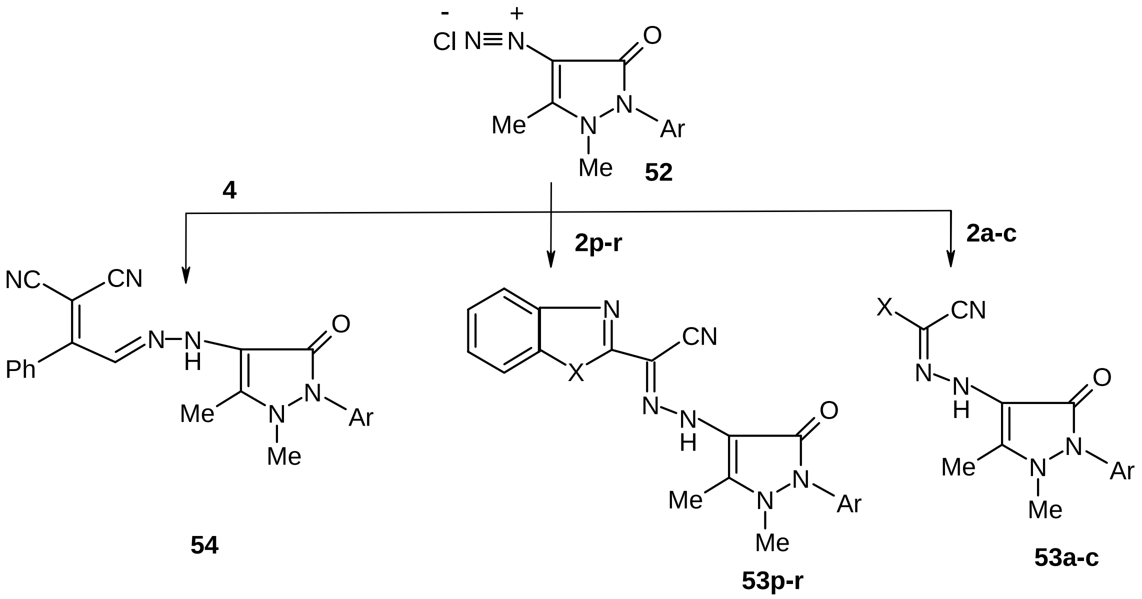
2.2. COUPLING ACTIVE METHYLENE COMPOUNDS HAVING CYANO GROUP WITH HETEROAROMATIC DIAZONIUM SALTS

Heterocyclic diazonium salts also readily couple with active methylene compounds yielding either arylhydrazones, that readily cyclize into aminoazoloazine or directly azoloazines depending on the nature of the utilized amine. Coupling diazotized aminopyrazoles **42** with active methylene reagents gave the corresponding acyclic hydrazones that readily cyclized under mild condition into the corresponding azolotriazines **48-51** (cf. Scheme 9).[43, 65-80]



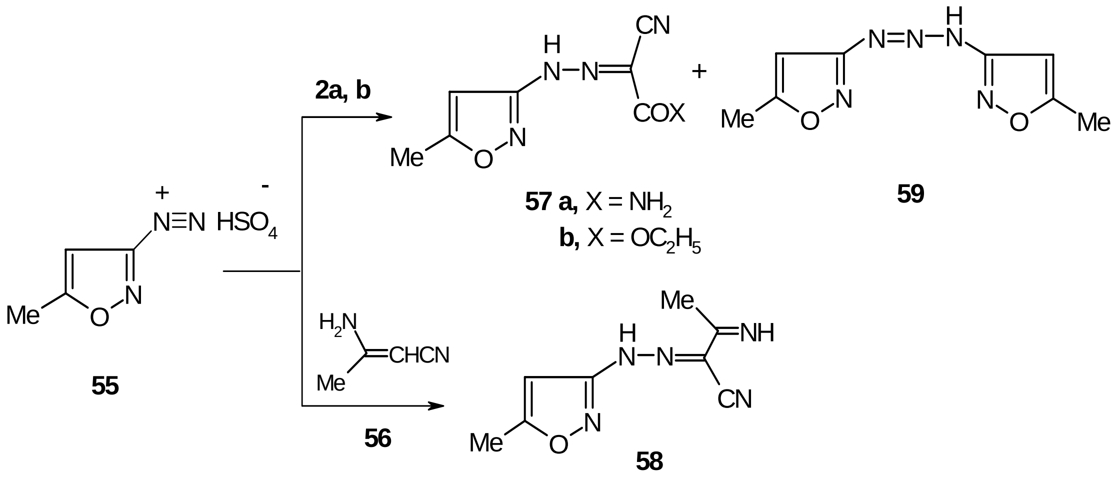
Scheme 9

Also diazotized aminoantipyrene **52**[43,81-82] readily couple with active methylene compounds yielding the corresponding hydrazones **53-54** (cf. Scheme 10).



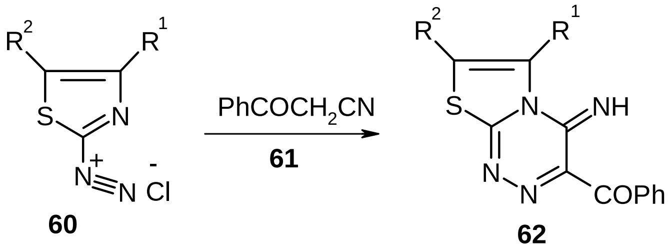
Scheme 10

It has been found that 3-amino-5-methylisoxazole[83] is readily diazotized by sodium nitrite and sulphuric acid to afford the corresponding diazonium salt **55** which easily coupled with **2a,b** and 2-aminocrotononitrile **56** to afford the corresponding hydrazones **57a,b** and **58**. In case of coupling **55** with **2a** and **2b** the diazoaminoisoxazole derivative **59** was also formed in addition to the corresponding hydrazones (cf. Scheme 11).



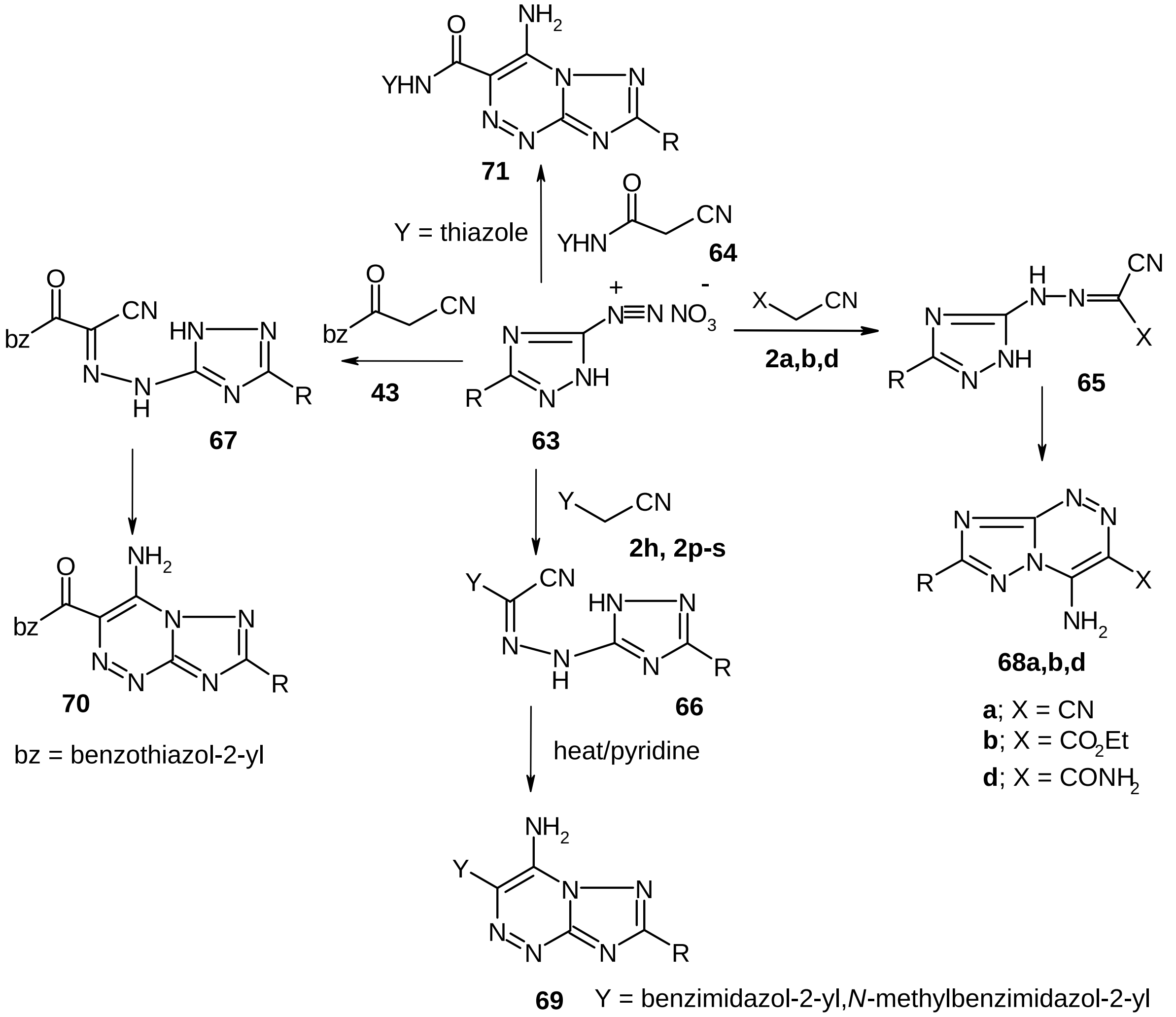
Scheme 11

Diazotized aminothiazole derivative **60**[84] coupled with benzoylacetonitrile **61** to give thiazolo[2,3-*c*] [1,2,4] triazine derivative **62** (cf. Scheme 12).



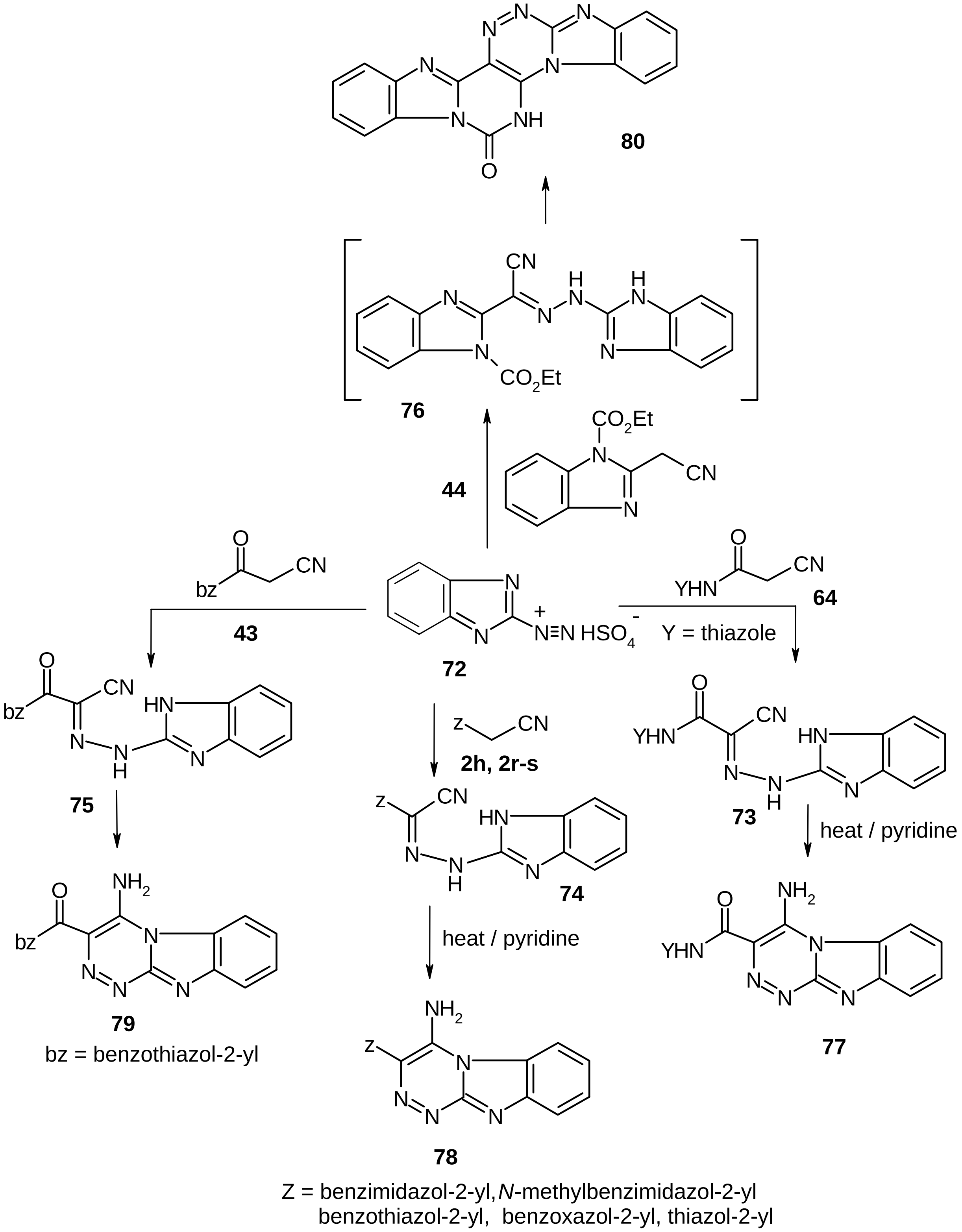
Scheme 12

Coupling of 1*H*-1,2,4-triazole-5-diazonium nitrate **63**[80,84-85] with active methylene compounds gave the corresponding azolotriazines **68-71** (cf. Scheme 13).



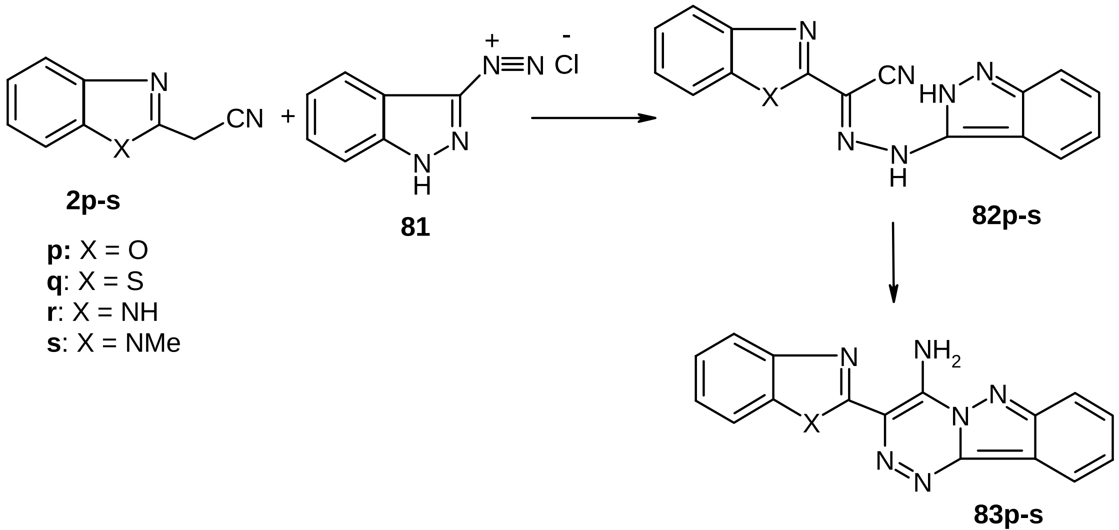
Scheme 13

In a similar manner 1*H*-benzimidazole-2-diazonium sulfate **72**[79,80,85] couples with acetonitrile derivatives to afford firstly the acyclic hydrazones **73-76** which then cyclized intramolecularly when heated in pyridine to the corresponding benzoazolotriazine derivatives **77-80** (cf. Scheme 14).



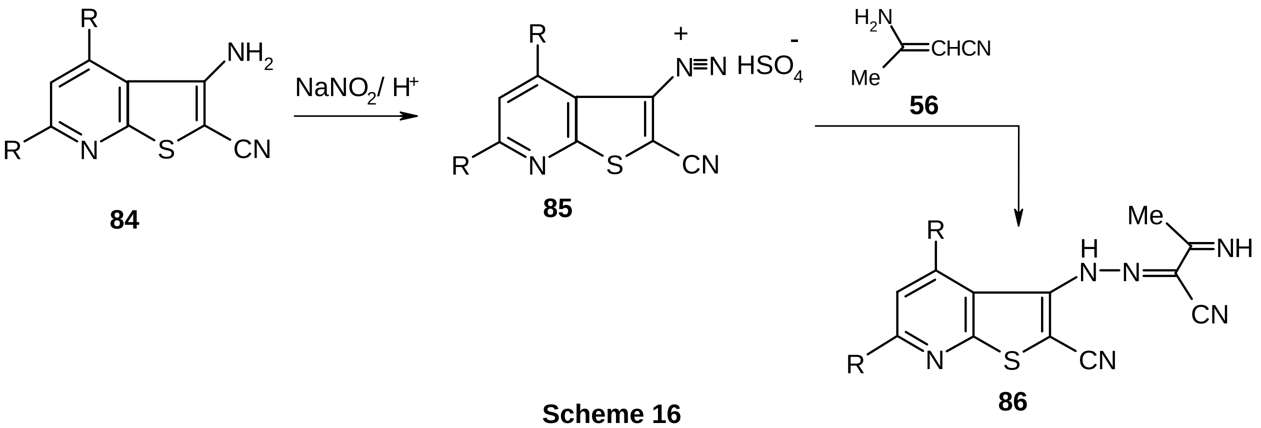
Scheme 14

Similarly, indazole-3-diazonium chloride **81**[80] also coupled readily with **2p-s** to afford the expected hydrazones **82p-s** in a high yields. Heating the hydrazones **82p-s** in pyridine, gave the corresponding 1,2,4-triazino[4,3-b]indazole derivatives **83p-s** (cf. Scheme 15).



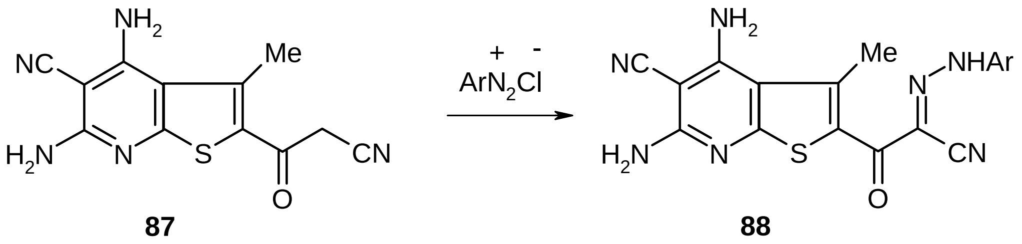
Scheme 15

The 3-amino-2-cyano-4,6-disubstitutedthieno[2,3-*b*]pyridines (**84**) can be diazotized with sulphuric acid to afford the diazonium sulfate **85** which coupled with 3-aminocrotononitrile **56** in sodium acetate buffered solution to give the thieno[2,3-b]pyridines **86**[86] (cf. Scheme 16)**.**



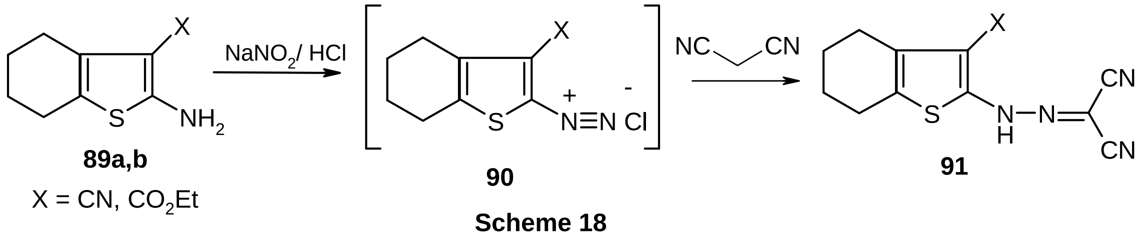
Scheme 16

Furthermore, thieno[2,3-*b*]pyridines **87** coupled with aromatic diazonium salts to afford the corresponding arylhydrazone derivatives **88**[87] (cf. Scheme 17).



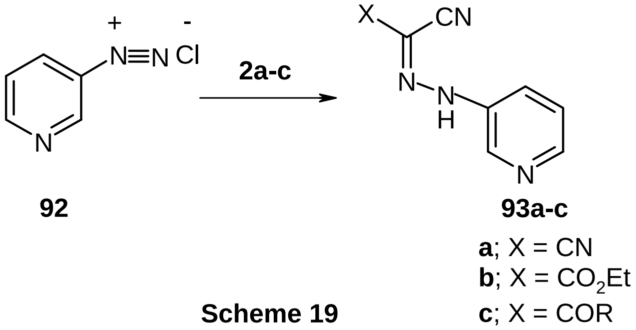
Scheme 17

Similarly diazotizing **89** in presence of hydrochloric acid gives **90** that coupled with malononitrile to yield **91**[88, 89] (cf. Scheme 18).



Scheme 18

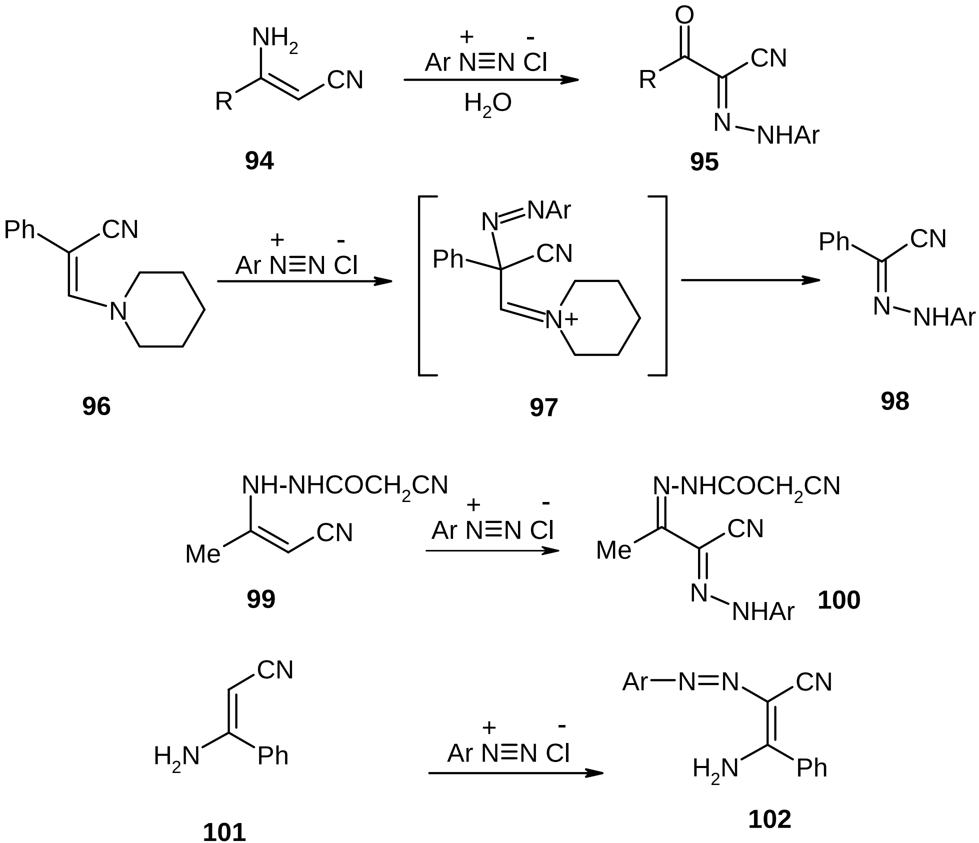
Diazotized 3-aminopyridine **92**[90] behaves in similar manner towards active methylene compounds to give the corresponding hydrazones **93** (cf. Scheme 19).



Scheme 19

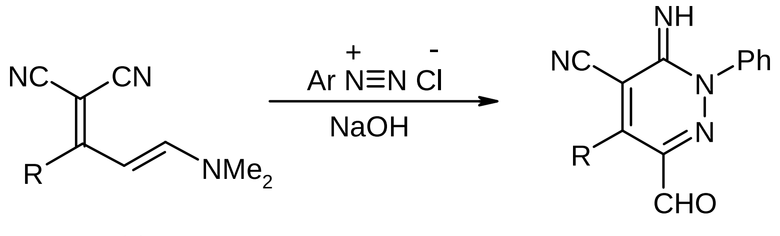
2.3. COUPLING OF ENAMINONITRILES WITH AROMATIC DIAZONIUM SALTS

Enaminonitriles coupled with aromatic diazonium salts to yield the corresponding 2-arylhydrazono-3-oxoalkanenitriles **95**[5] or 2-arylhydrazonoalkane nitriles[91-93] **98**, **100** and **102** (cf. Scheme 20).



Scheme 20

Coupling 2-cyano-5-dimethylamino-3-substitutedpent-2,4-dienonitriles **103** with benzenediazonium chloride in ethanolic sodium hydroxide gives the pyridazinals **104**[94] (cf. Scheme 21).

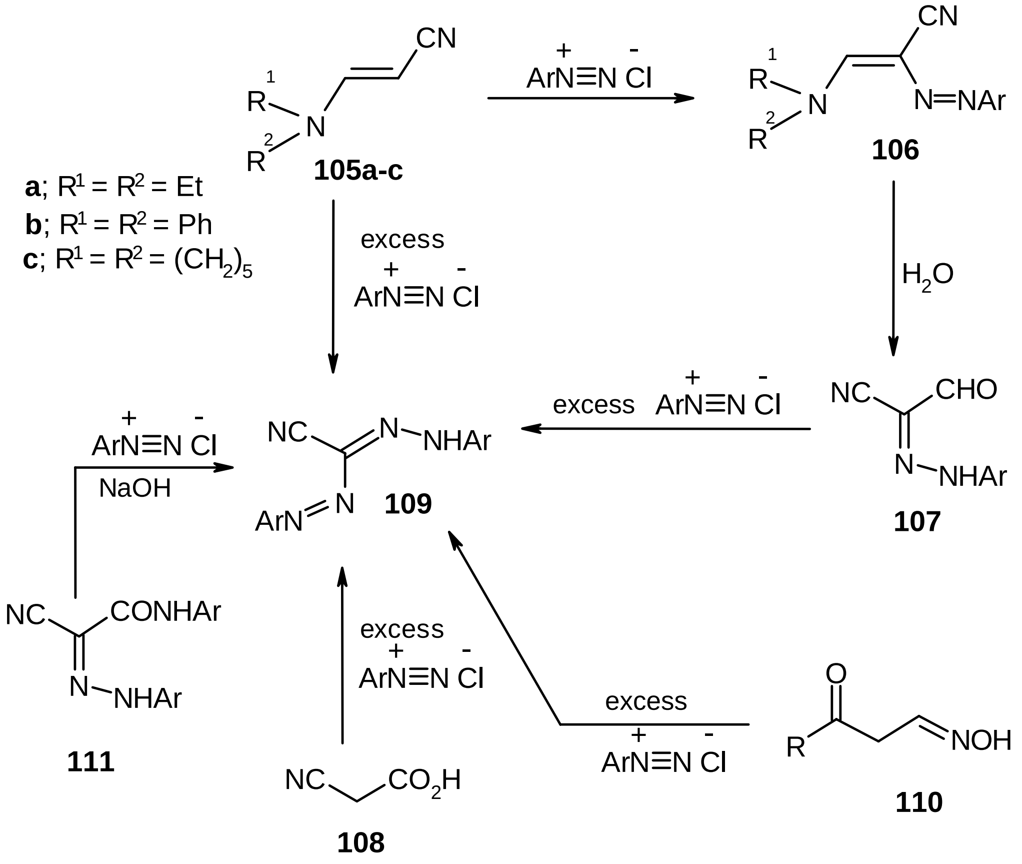


103

104

Scheme 21

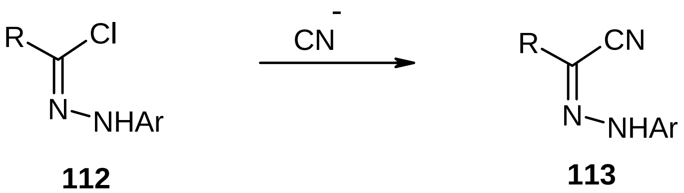
The coupling of **105a-c** with aromatic diazonium salts gives **107** *via* **106** which could be isolated in some cases.[95,96] The coupling of cyanoacetic acid **108** with aromatic diazonium salts give formazanes **109**[97] that are also produced through coupling **105a-c** or **107** with excess aromatic diazonium salts.[95,96] Also the formazanes **109** could be obtained *via* coupling the aldoximes **110** with excess aromatic diazonium salts,[98] or similarly by coupling the arylazo cyanoacetarylamides **111** with aromatic diazonium salts in sodium hydroxide[20] (cf. Scheme 22).



Scheme 22

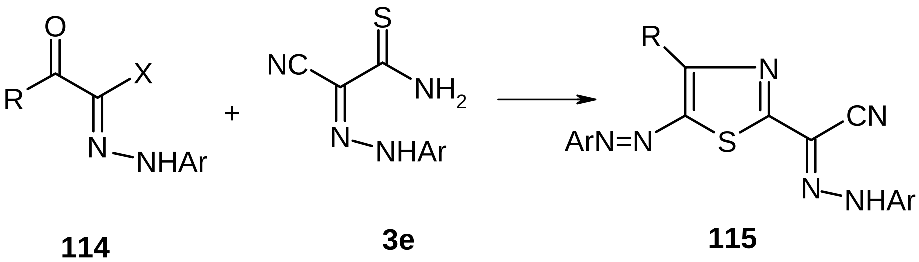
2.4. REACTIONS WITH HYDRAZONOYL HALIDES

Shawalli *et al.*[99-101] have reported formation of **113** from reaction of **112** with cyanide ion.[102] The reaction was conducted in ethanolic solution at room temperature (cf. Scheme 23).



Scheme 23

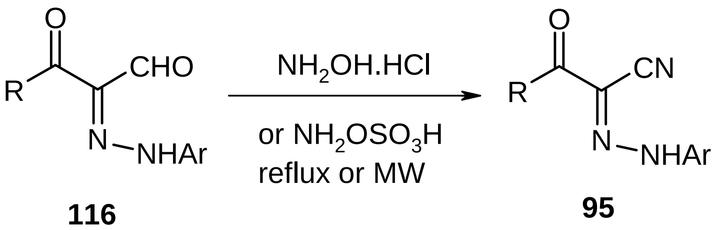
Treatment of 2-oxohydrazonoyl halides **114**[26,103] with 2-arylhydrazonocyanothioacetamide (**3e**) yielded the azo derivatives **115** (cf. Scheme 24).



Scheme 24

2.5. REACTION OF ARYLHYDRAZONOALKANAL WITH HYDROXYLAMINE

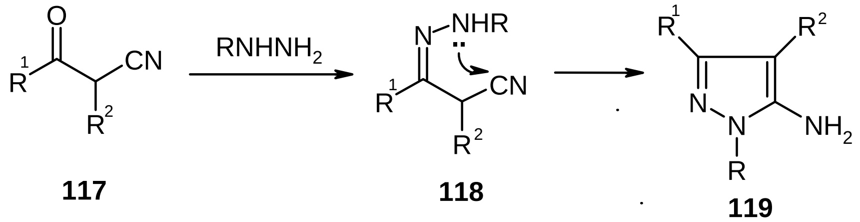
Recently Elnagdi *et al.*[98,103-108] could efficiently synthesis 3-oxo-2-aryl-hydrazonoalkanenitriles **95** from the reaction of arylhydrazonals **116** with hydroxylamine hydrochloride or hydroxylamine-*O*-sulphonic acid under thermal and microwave irradiation (cf. Scheme 25).



Scheme 25

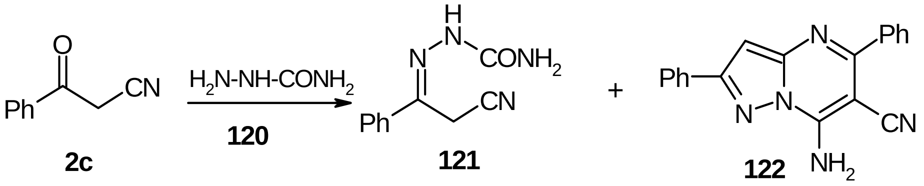
2.6. CONDENSATION OF OXOALKANENITRILES WITH HYDRAZINES (PREPERATION OF β- AND γ-HYDRAZONONITRILE)

3-Oxoalkanenitriles **117** condense with arylhydrazines yielding the arylhydrazone derivatives **118** that readily cyclized into the corresponding 5-aminopyrazole derivatives **119**[99,109-113] (cf. Scheme 26).



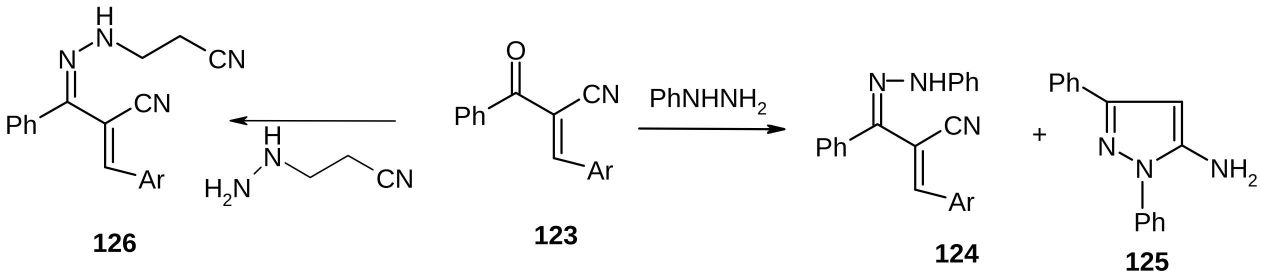
Scheme 26

Sprio and Fabra[114,115] have investigated the reaction of semicarbazide hydrochloride **120** with benzoylacetonitrile **2c** and have shown that the product, is really 3-phenyl-3-oxopropanenitrile semicarbazone (**121**). The other product, was proved to be the pyrazolo[2,3-*a*]pyrimidine derivative **122** (cf. Scheme 27).



Scheme 27

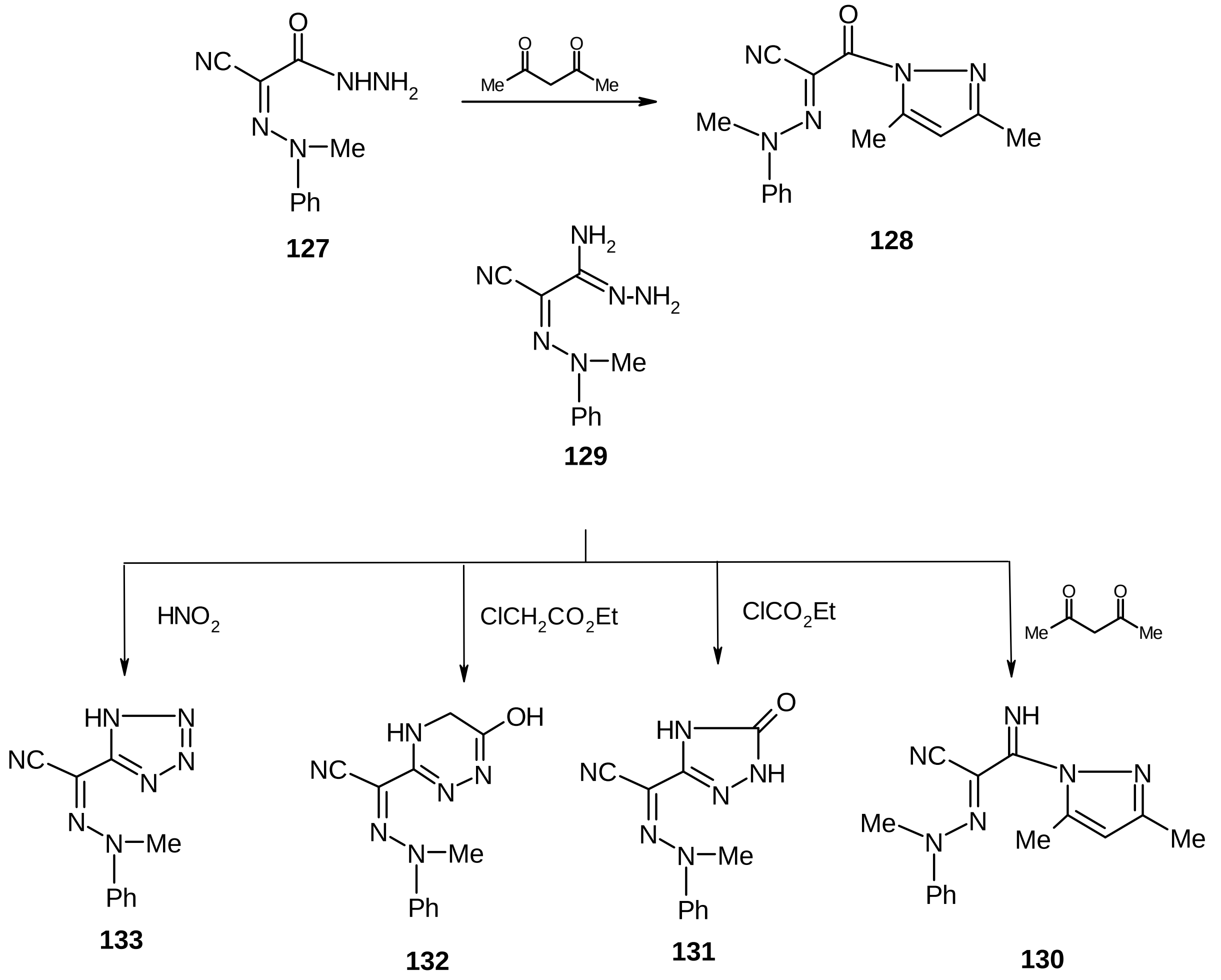
The arylidene derivatives of 3-oxopropanenitrile **123** were reported to condense with phenylhydrazine to give the isolable phenylhydrazone intermediates **124** together with the aminopyrazole **125.**[114,116-119] Elnagdi *et al.*[120-122] have reported that **123** reacts with *β*-cyanoethylhydrazine to yield the isolable hydrazones **126**. (cf. Scheme 28).



Scheme 28

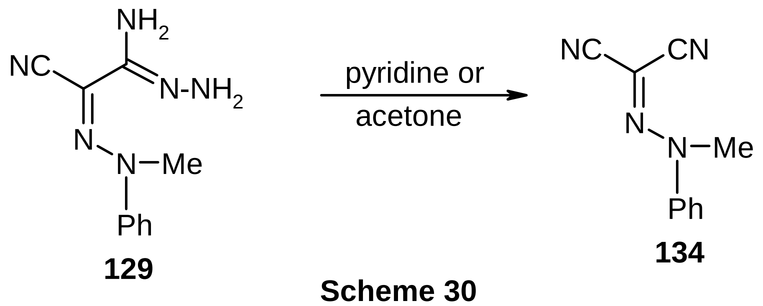
2.7. MISCELLANEOUS SYNTHETIC APPROACHES

A variety of new heterocyclic hydrazonoalkanenitriles can be prepared from the hydrazide **127** and amidrazone **129**. For example both hydrazide **127** and amidrazone **129** reacted with acetylacetone yielding the pyrazole derivatives **128** and **130** respectively.[123] On the other hand amidrazone **129** reacted with ethyl chloroformate, ethyl chloroacetate and nitrous acid to yield the corresponding 1,2,4-triazole derivative **131**, 1,2,4-triazine derivative **132** and 1,2,4-tetrazole derivative **133** respectively[123] (cf. Scheme 29).



Scheme 29

Heating the amidrazone **129** in pyridine or in acetone for long period it was converted into the hydrazone **134**[22] (cf. Scheme 30).



Scheme 30

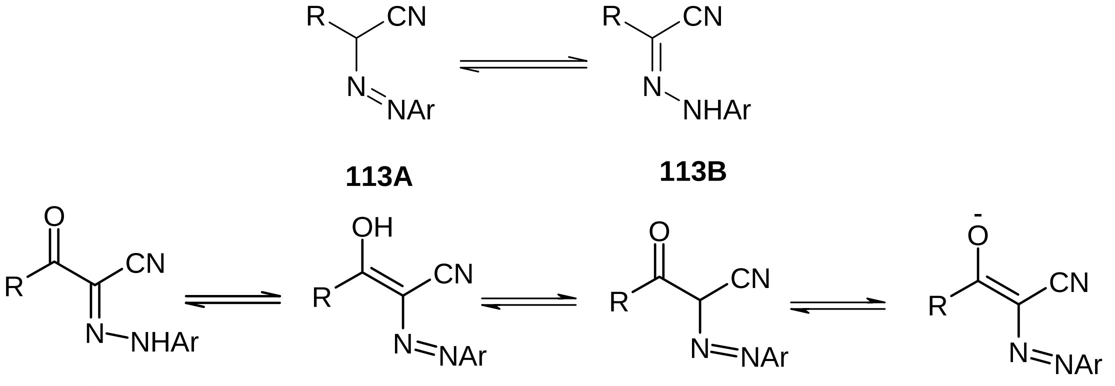
Refluxing **135** in a dioxane/acetonitrile mixture resulted in the formation of the hydrozonyl bromide **136**[34] (cf. Scheme 31).

135 **136**

Scheme 31

3. STRUCTURAL STUDIES ON HYDRAZONONITRILES

Plenty of investigation on structure of arylhydrazononitriles has been made. Arylhydrazononitriles may in theory exist in the azo form **113A** or the hydrazone form **113B** and in case of the presence of carbonyl functional substituents an added enol azo form **95B** may be also drawn beside the keto form **95A**. From time to time several authors have presented data in favour of one or more of these forms or suggested presence of an equilibrium mixture of more than one form. However it was established long ago that these compounds prefer the hydrazone form **113B**. Elnagdi *et al.* have used polargraphy to investigate the structure of these compounds, while a detailed discussion of ^{1}H NMR spectra of several oxoalkanenitrile derivatives has been made. Elnagdi and his colleges have suggested,[5,7,8,124-132] based on polargraphic data and the effect of substituents on the polargraphic and the acid dissociation constants, that compound **113B** exist in ethanolic solutions at pH< 4 in the hydrazone form. At pH > 4, these compounds were shown to exist as an equilibrium mixture of the arylhydrazone **113B** and the resonance stabilized anion. Recent studies utilizing dipole moment measurements and calculation of the theoretical dipole moment of each of the forms **95A-D** indicated that these compounds can be best presented in the solid state and in inert solvents as the zwitterion **95D**[128] (cf. Chart 2).



113A **113B**

95A **95B** **95C** **95D**

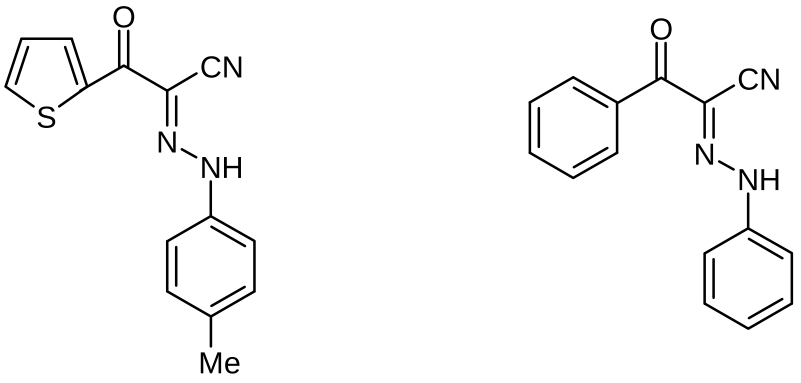
Chart 2

Perlin *et al.*[133] has observed that these hydrazones having low field NH signal at δ 12-14, and so they suggested the presence of the *syn* hydrogen bonded form **95A** to account for the observed deshielding effect of the hydrazones NH in the ^{1}H NMR spectra. The stability of this form over the possible *anti* form **95A** was attributed to the effect of the hydrogen bonding (Chart 3).

95A (*syn*) **95A (*anti*)**

Chart 3

Recently however Elnagdi *et al.*[134] have obtained X-ray data for several oxoalkanonitrile derivatives and could show that in contrast to a general assumption of presence of *syn* hydrogen bonded forms actually these compounds did exist in the *anti* form **95A**. This clearly indicated that stereoeletronic effect overweight possible fixation by the hydrogen bonding. Elnagdi *et al.*[135] reported X-ray crystal structure for **137**, it was noted that the molecule is planar and adopts *anti* configuration for hydrazone and carbonyl function. It is of value to note also that S and O are also *anti* to each other. This lead to conclusion that the streoelectronic factors significantly overweigh possible hydrogen bonding fixation. As a result Hafez and Elnagdi[136] have also obtained X-ray structure for **138** which adopted *E*-form and the phenyl group now free from streoelectronic factors rotated and become almost perpendicular to the plane in most stable conformation (Chart 4).



137 **138**

Chart 4

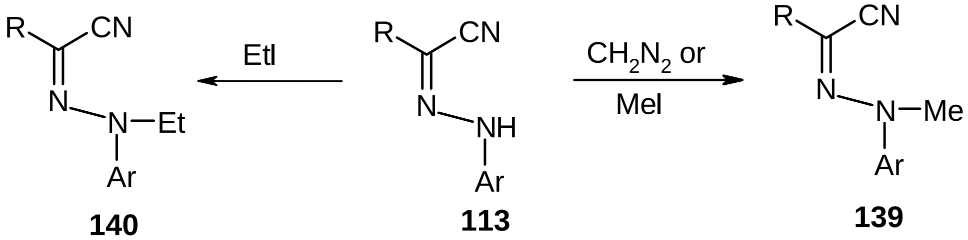
It can thus be concluded that the observed low field NH signal in ^{1}H NMR is in fact due to extensive delocalization of nitrogen atom lone pair rendering hydrazone carbon electron rich. In support of this view ^{1}H NMR of phenyhydrazonomesoxalonitrile showed NH signal at δ ~ 13.0 ppm. Here the hydrogen bonding is not possible.

4. CHEMICAL PROPERTIES OF HYDRAZONOALKANENITRILES

4.1. REACTION WITH ELECTROPHILIC REAGENTS

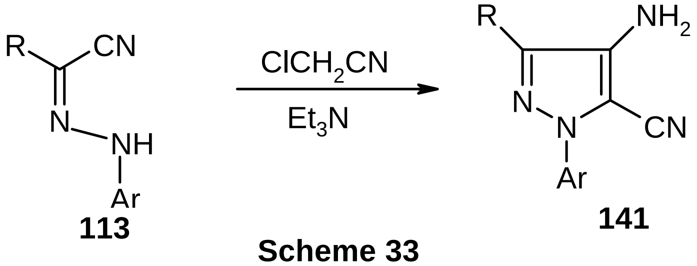
4.1.I. REACTION WITH CARBON ELECTROPHILES

The best investigated reaction is alkylation and reactions with diazomethane,[3,7] methyl iodide[22,137] and ethyl iodide[51] (cf. Scheme 32).



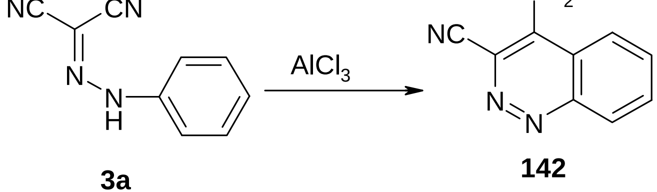
Scheme 32

Goncalves *et al.*[138] have reported that **113** could react successfully with chloroacetonitrile in presence of triethylamine producing 4-aminopyrazoles **141** (cf. Scheme 33).



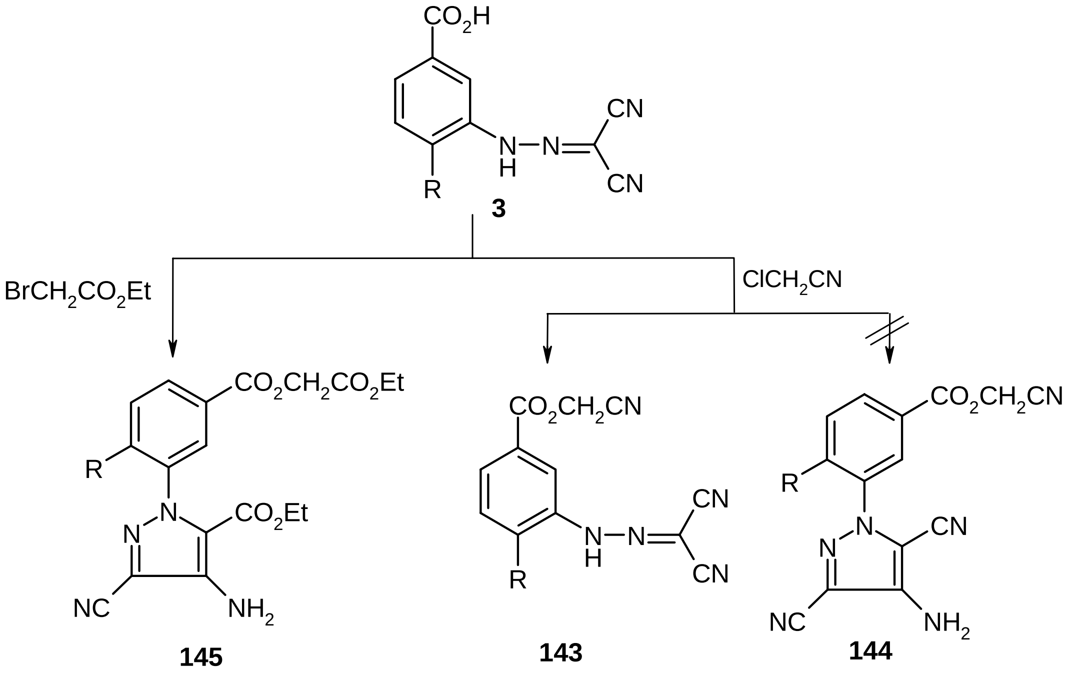
Scheme 33

Gewald and coworkers reported cyclization of **3a** in presence of nitrobenzene and anhydrous aluminum chloride (Friedel-Craft's conditions) into cinnolines **142**[139,140] (cf. Scheme 34).



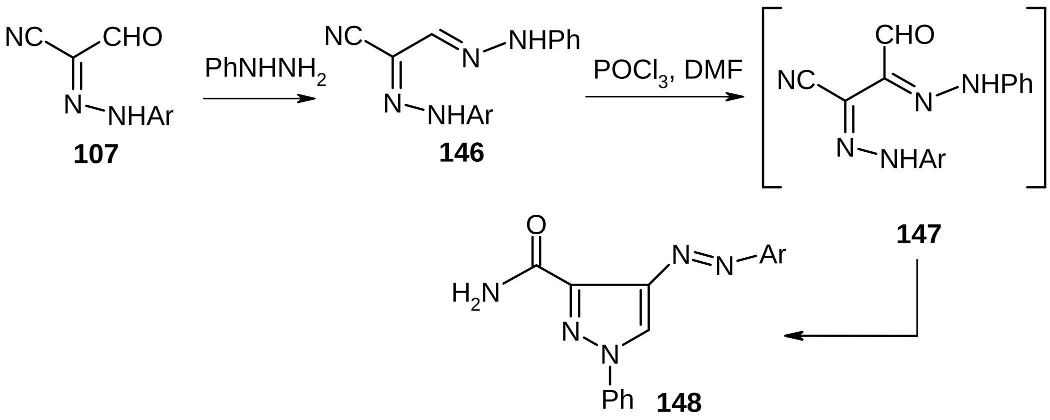
Scheme 34

When the hydrazononitrile **3** was treated with chloroacetonitrile, the open chain ester **143** was formed instead of the pyrazole **144**. However When **3** was treated with ethyl bromoethanoate, cyclization did occur and the 4-amino-3-cyano-5-ethoxycarbonylpyrazole derivatives **145** were obtained[141] (cf. Scheme 35).



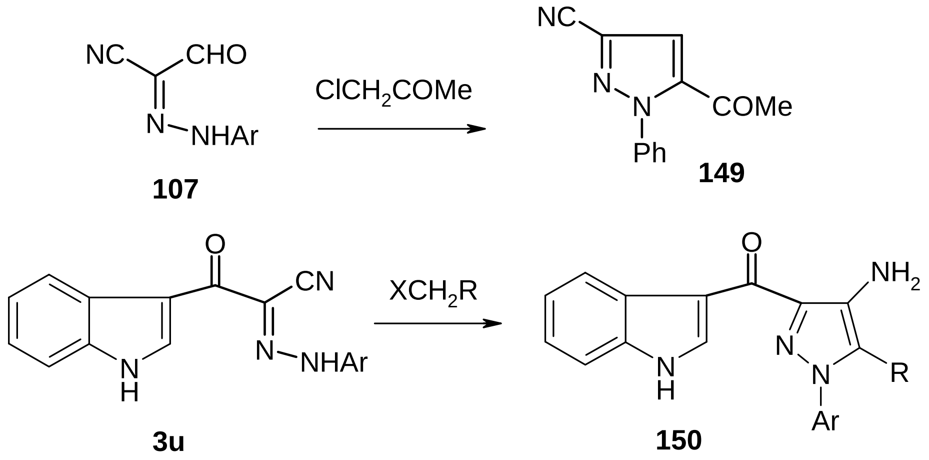
Scheme 35

The hydrazonoalkanals **107**[96] react with phenylhydrazine to yield the corresponding phenylhydrazone **146** in excellent yield under a variety of conditions. The latter was failed to cyclize into aminopyrazole derivatives. Recently Brehme *et al.*[142-145] has reported that aldehyde hydrazones are readily formylated on heating with phosphorus trichloride and dimethylformamide (Vilsmeier–Haack reagent). Also compound **146** was found to be readily formylated by the same reagent to yield a product that was formulated as the arylazopyrazole derivative **148** which is formed *via* the non isolable intermediate **147** (cf. Scheme 36).



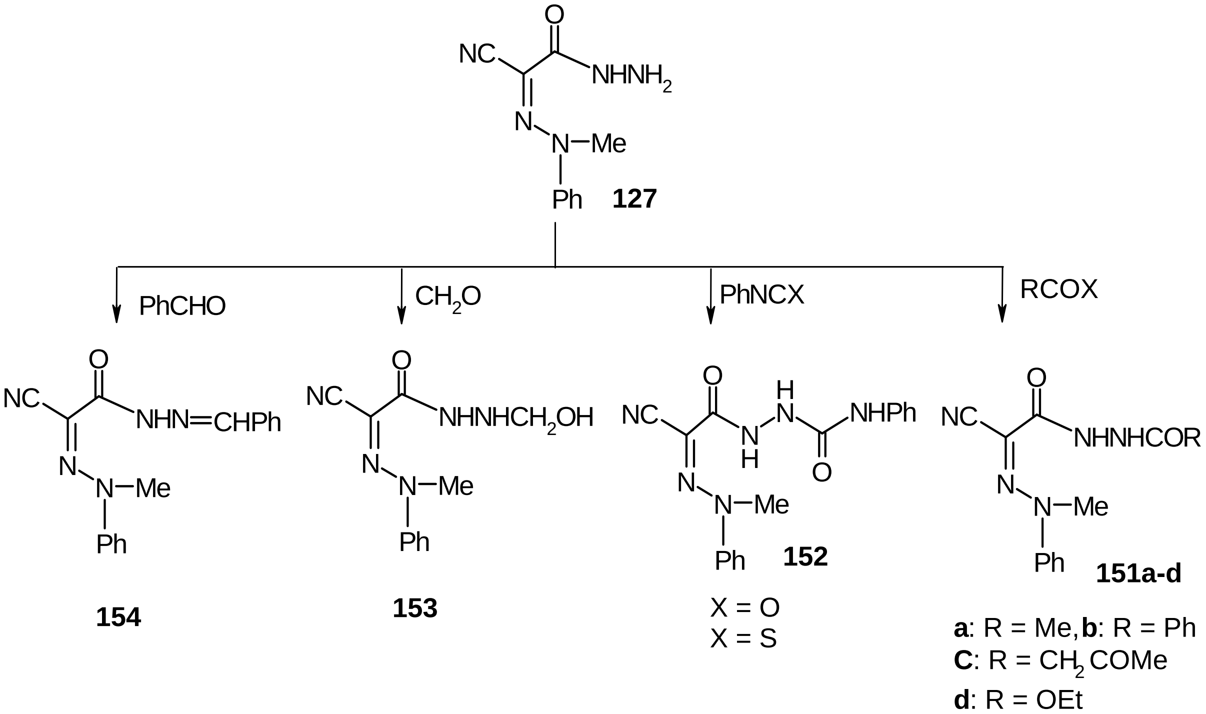
Scheme 36

Furthermore compound **107** reacts with chloroacetone to yield the pyrazole carbonitrile **149** which formed most likely *via* alkylation of **107** and subsequent cyclization.[96] 3-Oxo-2-arylhydrazonalkane nitrile **3u** also react with α-halo compounds to yield pyrazole derivatives **150**[146] (cf. Scheme 37).



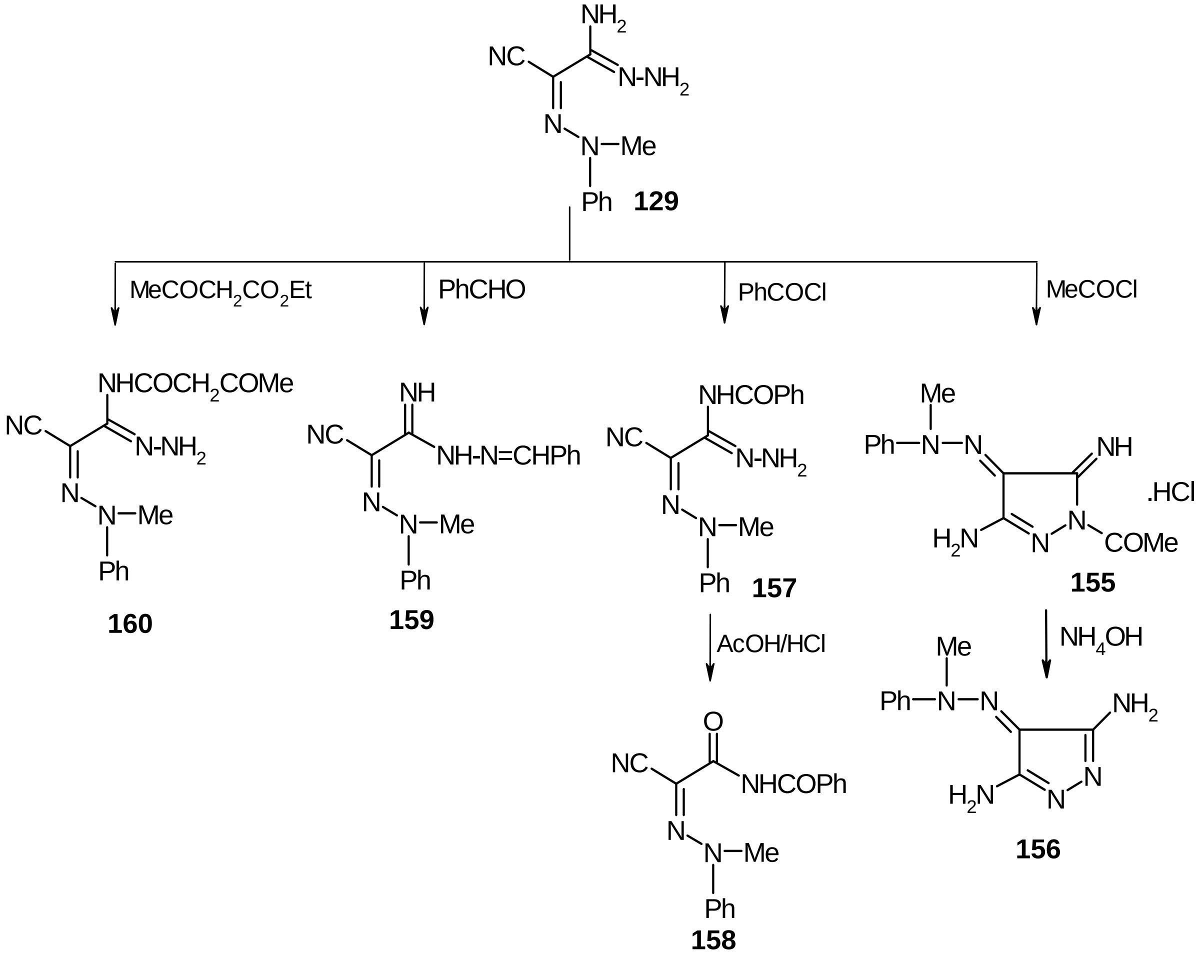
Scheme 37

The hydrazide **127** reacts with acyl halides to yield the acyl derivatives **151a-d**. Also the semicarbazide and thiosemicarbazide derivatives **152a,b** could be obtained *via* the reaction of **127** with phenylisocyanate and phenylisothiocyanate respectively. Compound **127** reacted with formaldehyde to yields the hydroxymethyl derivative **153** while it reacted with benzaldehyde affording the Schiff's base **154**[123] (cf. Scheme 38)**.**



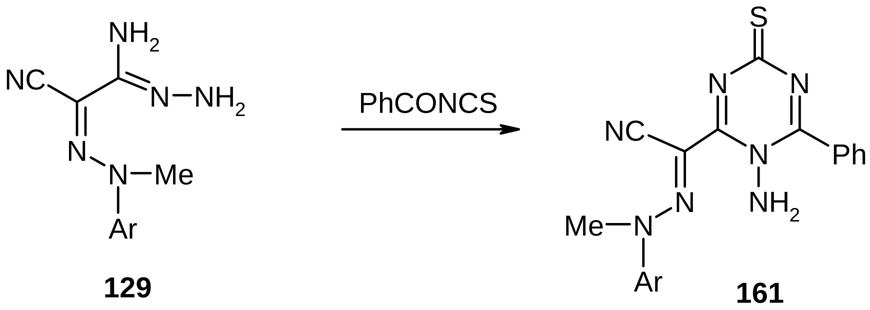
Scheme 38

In a similar manner the amidrazone **129** reacts with acetyl chloride to yield pyrazolimine derivative **155** which was converted into diaminopyrazole **156** by the action of ammonium hydroxide. Compound **129** reacted with benzoyl chloride to yield **158**, which is formed on refluxing **157** in acid. Also the amidrazone **129** condensed with benzaldehyde affording the corresponding Schiff's base **159**. Similarly compound **129** reacts with ethyl acetoacetate to yield a product for which structure **160** was assigned[123] (cf. Scheme 39).



Scheme 39

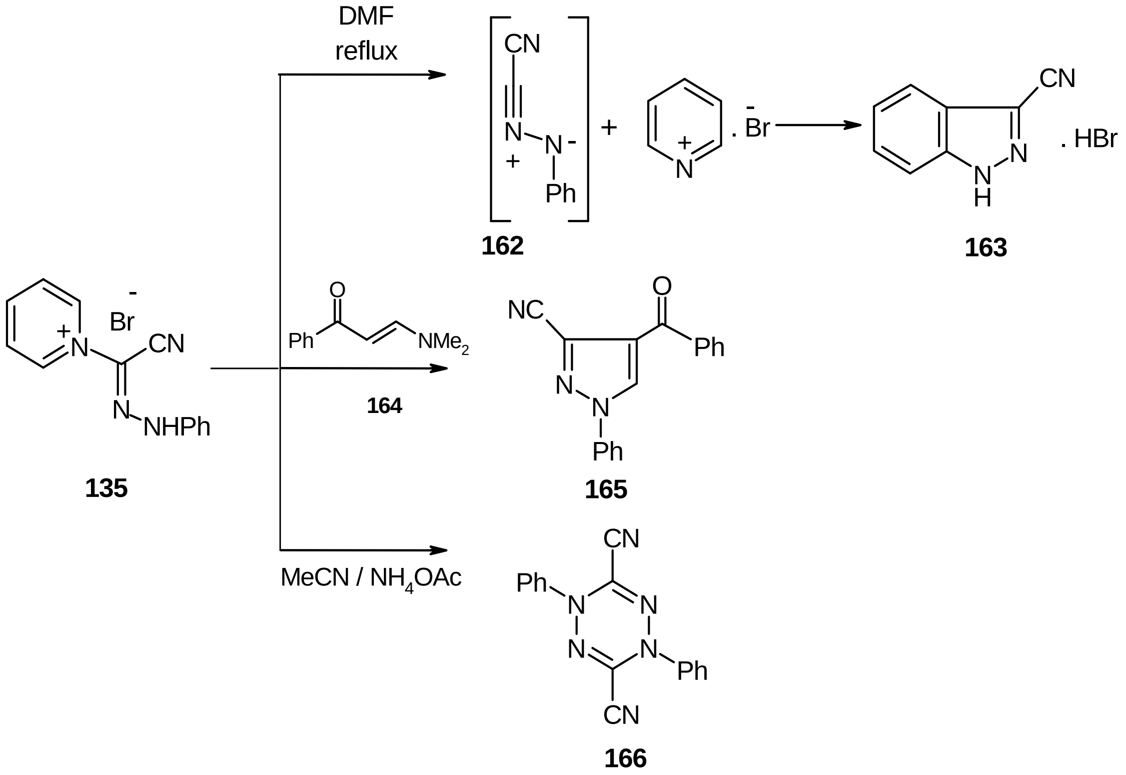
The amidrazone **129**[22] reacted with benzoylisothiocyanate in refluxing acetone to yield 1-aminotriazine derivatives **161** (cf. Scheme 40)**.**



Scheme 40

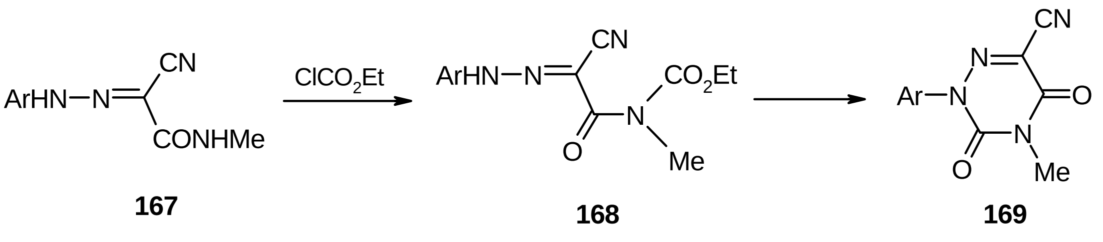
Compound **135** was converted into the cyanoindazole hydrobromide **163** when refluxed in dimethylformamide (DMF). The formation of this indazole derivative is believed to proceed through the intermediacy of the nitrilimine **162** which undergoes intramolecular cyclization into **163**, also fusion of **135** with the enaminone **164** afforded the pyrazole **165**. However compound **135**, was readily converted almost quantitatively upon reflux in acetonitrile in presence of ammonium acetate into the 1,4-diphenyl-

1,2,4,5-tetrazine **166**[34] (cf. Scheme 41).



Scheme 41

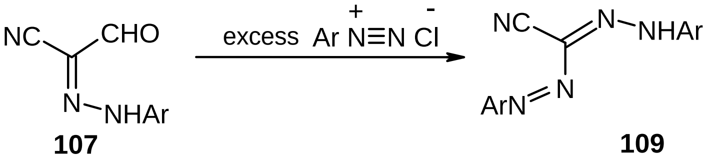
Slouka and Budkiora[147] reported synthesis of the triazine **169** *via* condensing the arylhydrazones **167** with ethyl chloroformate and subsequent cyclization of the resulting product **168**[148] (cf. Scheme 42).



Scheme 42

4.1.II. REACTION WITH NITROGEN ELECTROPHILES

Compound **107** couples with aromatic diazonium salts yielding the formazanes **109**[96] (cf. Scheme 43).

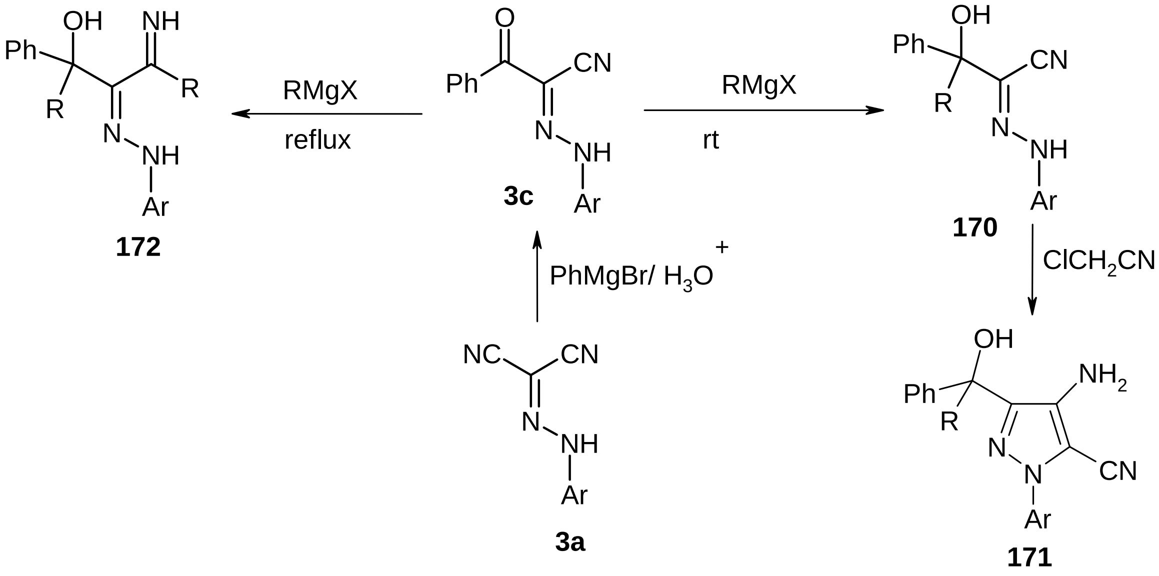


Scheme 43

4.2. REACTION WITH NUCLEOPHILIC REAGENTS

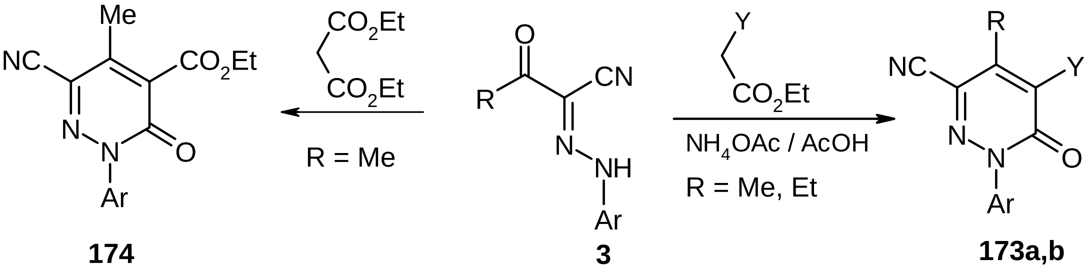
4.2.I. REACTION WITH CARBON NUCLEOPHILES

Elnagdi *et al.*[6,149,150] have reported on the behaviour of the 2-arylhydrazonoalkane nitriles **3c** toward Grignard reagents. It was shown that these arylhydrazone derivatives **3c** react with arylmagnesium halides in ether solution at room temperature (rt), to afford the carbinols **170**. Reaction of the latter with chloroacetonitrile afforded the corresponding 4-aminopyrazole derivative **171**. On the other hand, when the reaction of compound **3c** with arylmagnesium halides was conducted in refluxing benzene solution, addition of the Grignard reagent to both carbonyl and cyano moieties took place to yield the ketimino-carbinols **172**. It is worth to mention that; **3c** is formed from reaction of **3a** with Grignard reagent (cf. Scheme 44).



Scheme 44

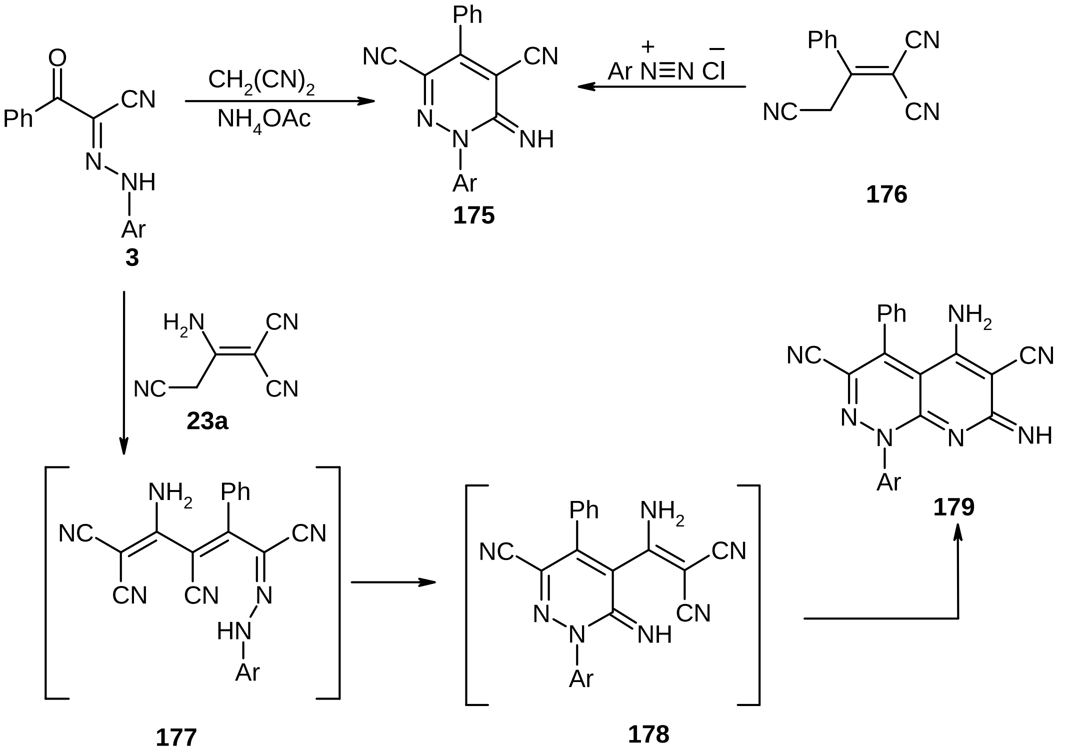
The pyridazin-6-oxo-3,5-dicarbonitrile derivatives **173a**[149-157] and pyridazin-3- carbonitrile **173b**[152,153] are prepared *via* condensation of the arylhydrazonoalkane nitriles **3** with ethyl cyanoacetate and ethyl benzoylacetate respectively in presence of ammonium acetate. Also condensation of **3** with diethyl malonate affords the corresponding ethyl pyridazine- carboxylate **174**[154, 155] (cf. Scheme 45).



173a; Y = CN
173b; Y = COPh

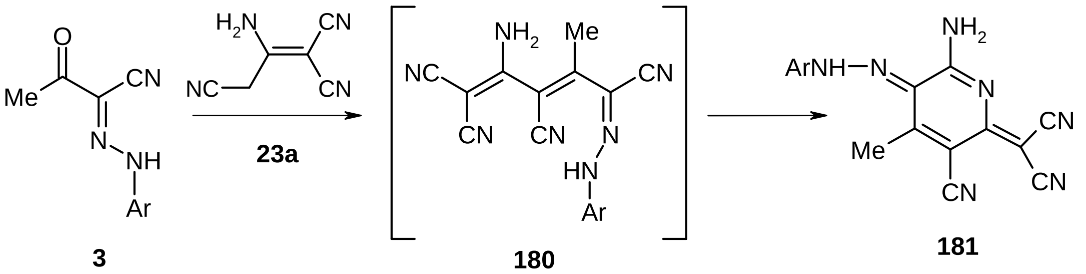
Scheme 45

Fusion of the arylhydrazono nitriles **3** with malononitrile in presence of ammonium acetate affords the pyridazin-6-imine derivatives **175**.[158] Compound **175** had been obtained earlier *via* coupling of **176** with aryldiazonium chloride. In a similar manner compound **3** also condensed with **23a** to yield the pyridopyridazines **179** presumably *via* the intermediacy of **177** and **178**[46,158-161] (cf. Scheme 46).



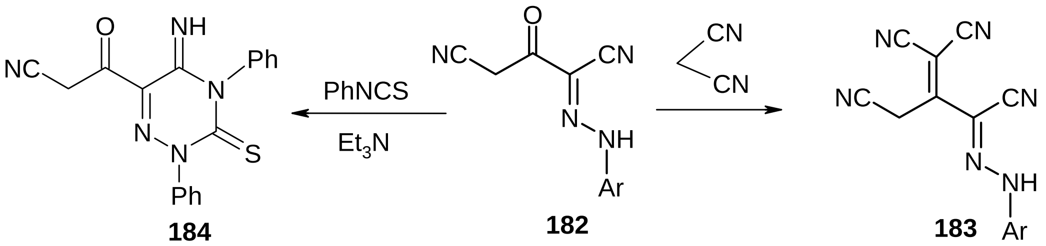
Scheme 46

Arylhydrazono nitrile **3** condenses with 3-amino-2-cyanopent-2-ene-1,5-dinitrile **23a** to yield aminopyridine derivative **181**[162,163] (cf. Scheme 47).



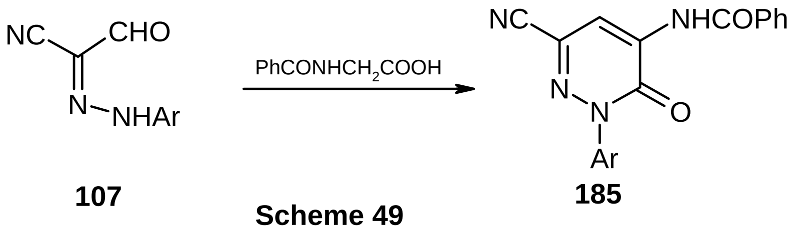
Scheme 47

Arylhydrazono nitrile **182** reacts with malononitrile to yield the condensation product **183**.[164] While reaction of **182** with phenylisothiocyanate in presence of triethylamine gave triazineimine derivative **184**[164] (cf. Scheme 48).



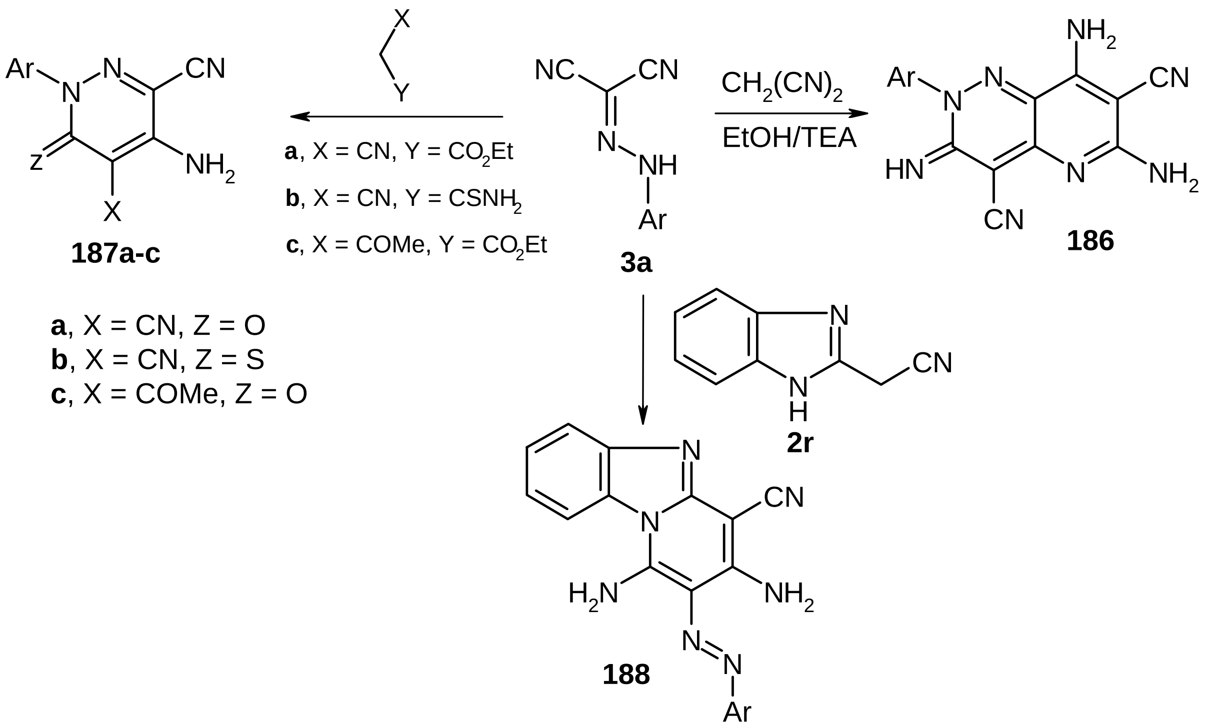
Scheme 48

The arylhydrazonalkanals **107** reacted with hippuric acid in refluxing acetic anhydride to yield **185**[96] (cf. Scheme 49).



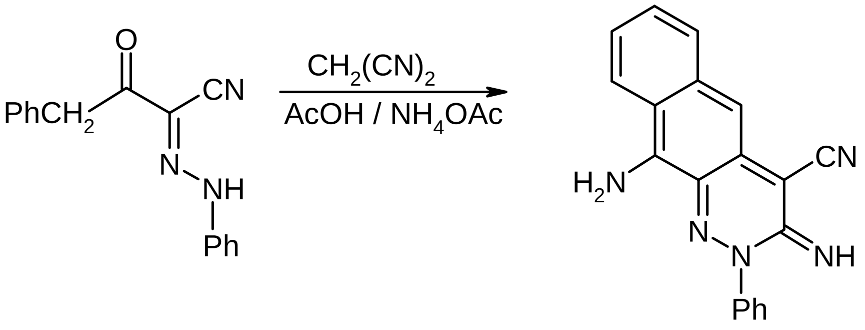
Scheme 49

The arylhydrazonomesoxalonitriles **3a** reacted with malononitrile in refluxing ethanol-triethylamine solution to yield the corresponding 1:2 adduct **186.**[158,161-164] In addition the reaction of **3a** with equimolar proportions of ethyl cyanoacetate, cyanothioacetamide and ethyl acetoacetate under the same experimental conditions affords the corresponding 4-aminopyridazine-3-carbonitrile derivatives **187a-c**.[165] Moreover, **3a** reacted with 2-cyanomethyl-1*H*-benzimidazole **2r** under reflux affording the benzimidazo[1,2-*a*]pyridine derivatives **188**[166] (cf. Scheme 50).



Scheme 50

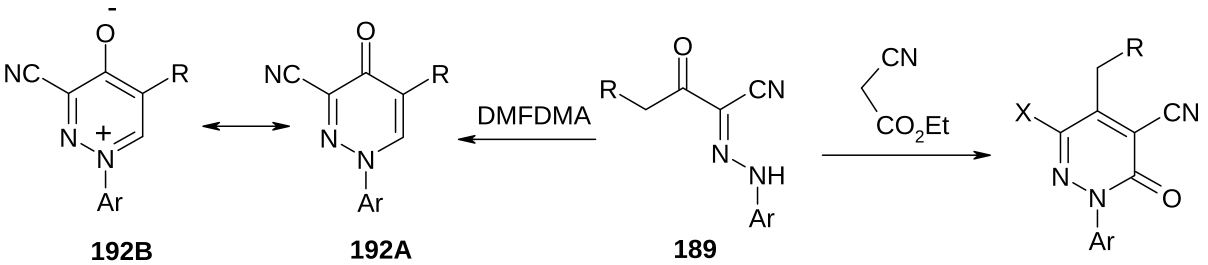
Reaction of phenylhydrazonoalkanenitrile **189** with malononitrile affording a product of condensation that formulated as **190**[167] (cf. Scheme 51).



189 **190**

Scheme 51

The reaction of **189** with ethyl cyanoacetate to yield **191a** required long reflux with azeotropic elimination of water resulted during condensation. If water was not eliminated the amide **191b**[154] was the sole isolable product. Condensing compounds **189** with dimethylformamide dimethylacetal (DMFDMA) gives pyridazinones **192A**. The IR spectra of this compound did not show any band for ring CO. This may indicate that this compound is really best represented as **192B**[154] (cf. Scheme 52).

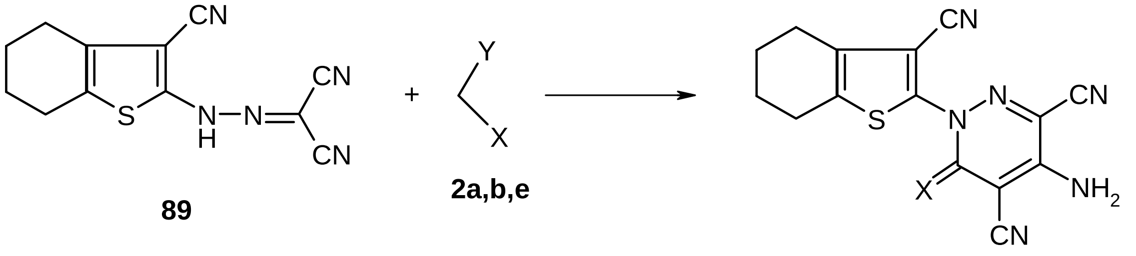


192B **192A** **189**

Scheme 52

191 a, X = CN
b, X = $CONH_2$

The hydrazonomesoxalonitrile **89** reacted with active methylene compounds **2a,b** and **2e** to afford a variety of substituted pyridazines **193a,b,e**[88] (cf. Scheme 53).

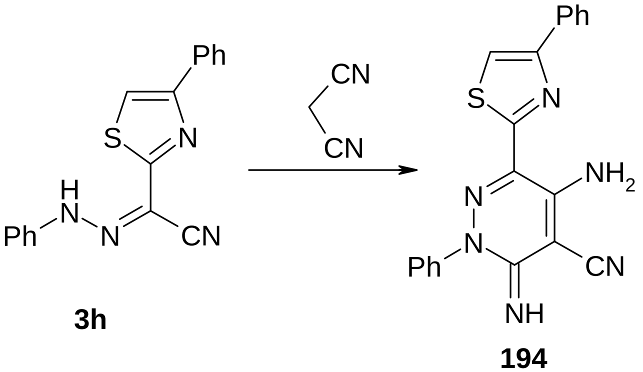


89 **2a,b,e** **193a,b,e**

a: X = NH; **b**: X = O; **e**: X = S

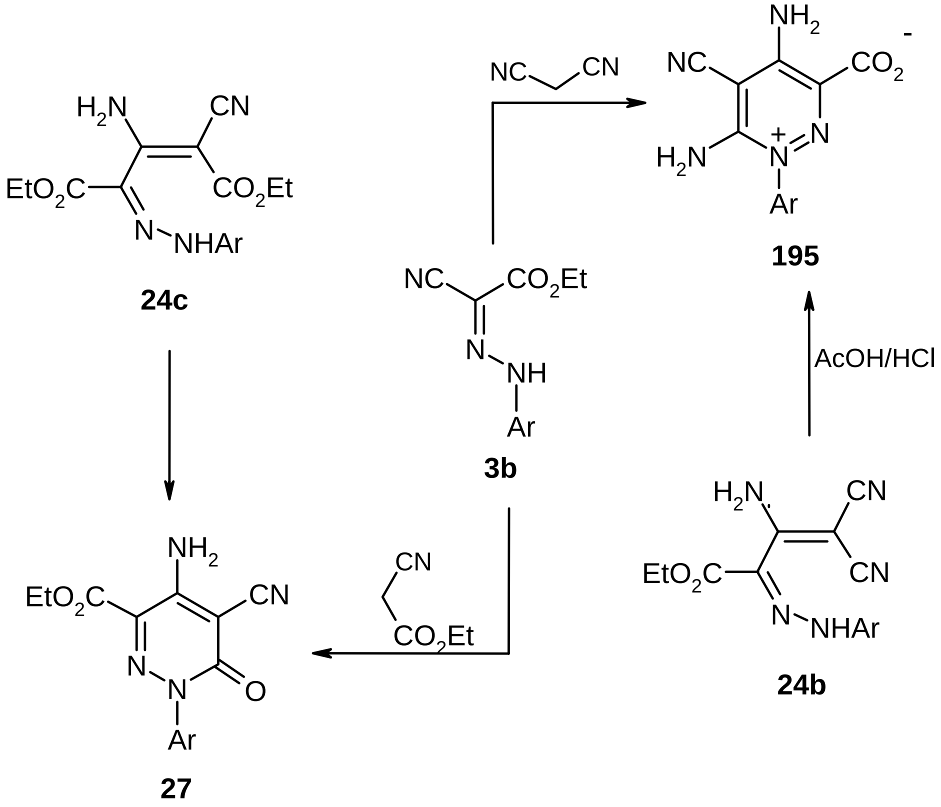
Scheme 53

Compound **3h** reacts with malononitrile in ethanolic triethylamine to yield the thiazolylpyridazin-6-imine derivative **194**[168] (cf. Scheme 54).



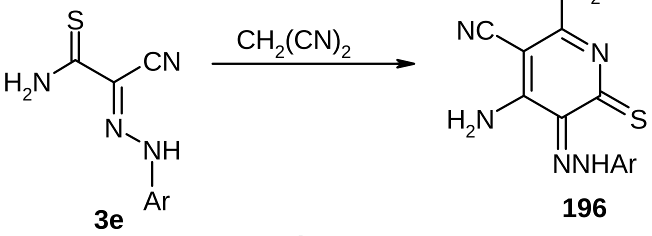
Scheme 54

Ethyl arylhydrazonocyanoacetate **3b** reacted with malononitrile in refluxing ethanolic aqueous triethylamine to yield the aminopyridazinium carboxylate **195** which could also be obtained by refluxing aryllhydrazone **24b** in acetic acid, hydrochloric acid mixture.[158] The arylhydrazonalkane nitrile **3b** reacted also with ethyl cyanoacetate to yield the pyridazin-6-one derivatives **27** which could also obtained by cyclization of the arylhydrazone **24c**[158,159] (cf. Scheme 55).



Scheme 55

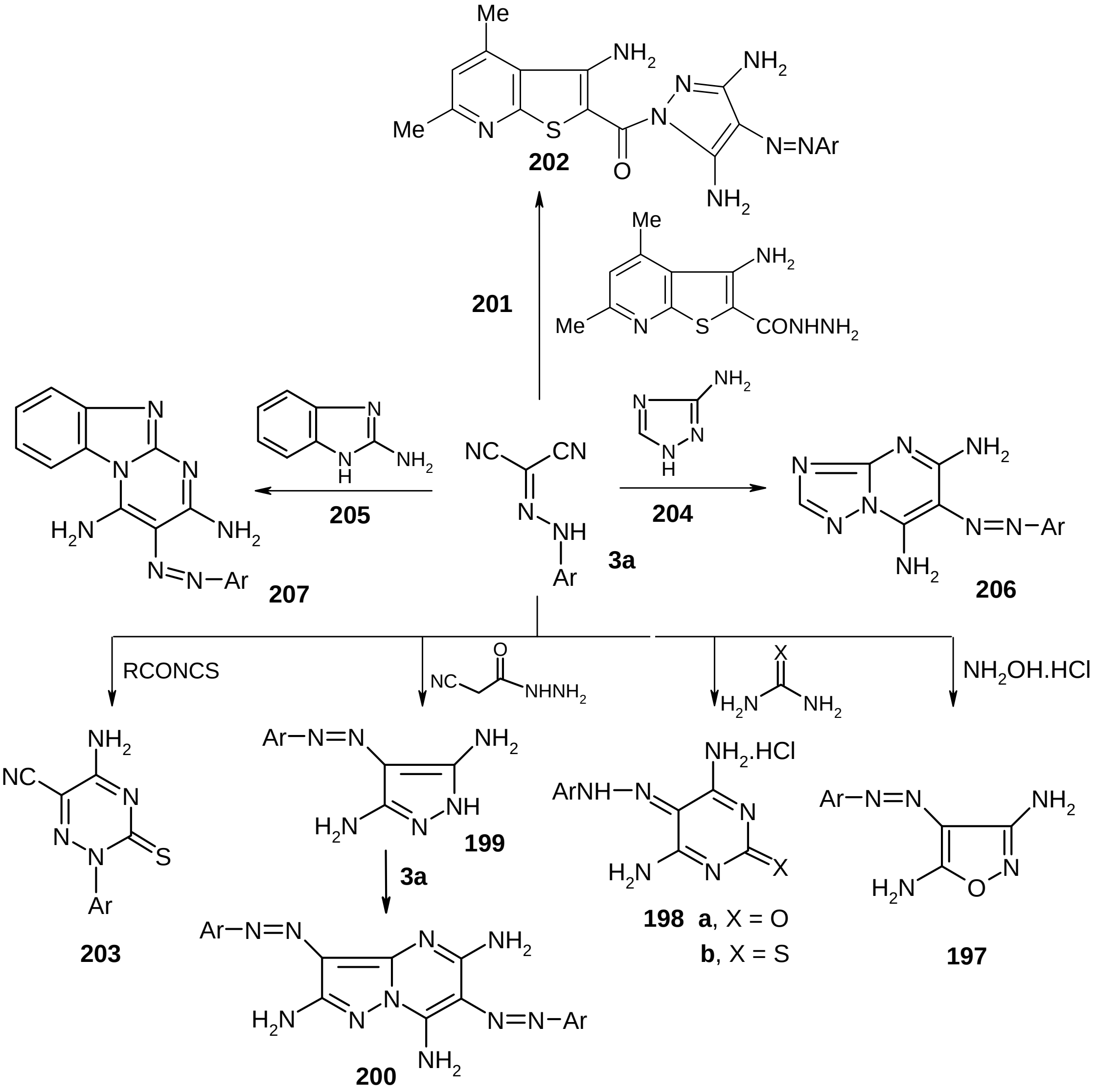
The reaction of **3e** with malononitrile affords 1:1 adduct which was assigned as the pyridinethione structure **196**[155] (cf. Scheme 56).



Scheme 56

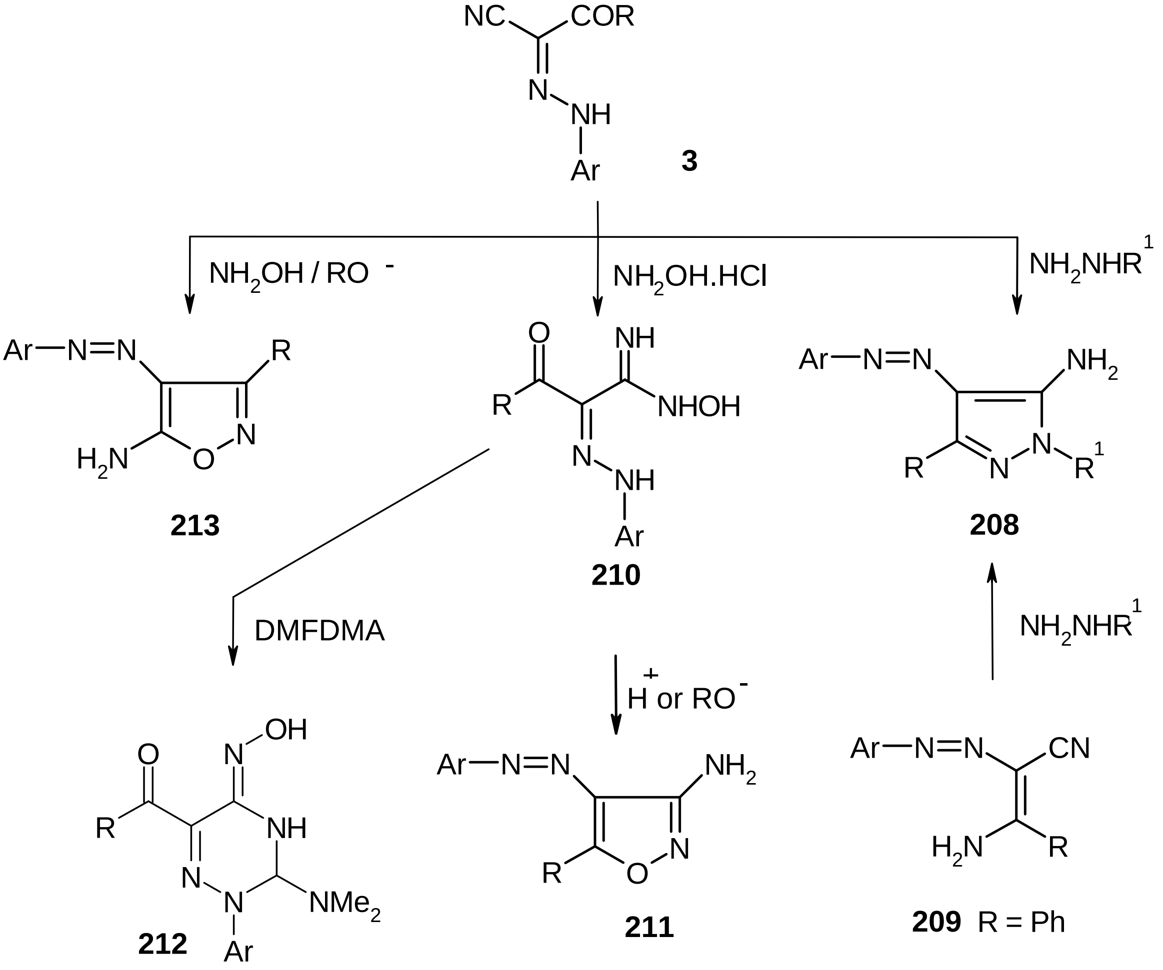
4.2.II. REACTION WITH NITROGEN NUCLEOPHILES

The arylhydrazonomesoxalonitriles **3a** reacted with a variety of amine derivatives such as hydroxylamine hydrochloride,[169] urea or thiourea,[51] cyanoacetohydrazide,[166,170] carbohydrazide,[171] benzoylisothiocyanate,[51] and aminoheterocyclic compounds[166] to afford arylazo-3,5-diaminoisoxazole **197**, pyrimidines **198**, pyrazolo[1,5-*a*]pyrimidines **200**, pyrazoles **202**, 1,2,4-triazines **203**, and azolopyrimidines **206** and **207** respectively (cf. Scheme 57).



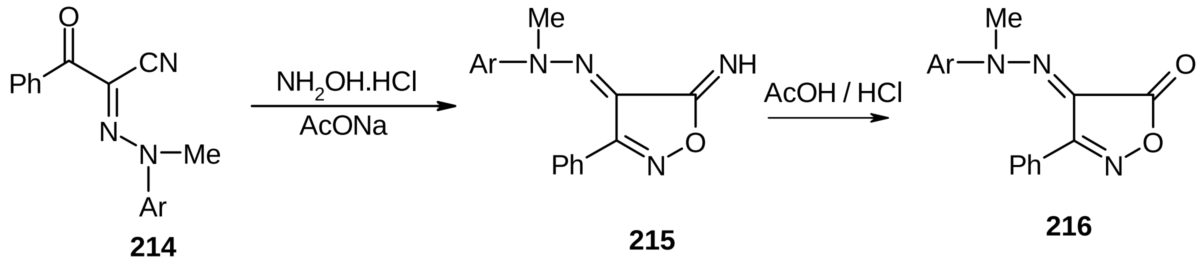
Scheme 57

A variety of arylhydrazonoalkanenitrile **3** react with hydrazines to afford the corresponding aminopyrazole derivatives **208**[84,92,99,104,105,167,172] Also the arylazoenaminonitrile **209** reacted with hydrazines to afford the same aminopyrazole.[93] Moreover, compound **3** reacts with hydroxylamine hydrochloride and sodium acetate in refluxing ethanol to yield the amidoximes **210**. 3-Amino-4-arylazo-5-substituted-isoxazoles **211** are formed when compound **210** was treated with acids or alkoxides.[173] Reacting **210** with dimethylformamide dimethylacetal afforded triazine derivative **212**.[104,105] On the other hand, treatment of **3** with hydroxylamine hydrochloride in the presence of excess methanolic sodium methoxide resulted in the formation of 5-amino-4-arylazo-3-substituted-isoxazoles **213** (cf. Scheme 58).



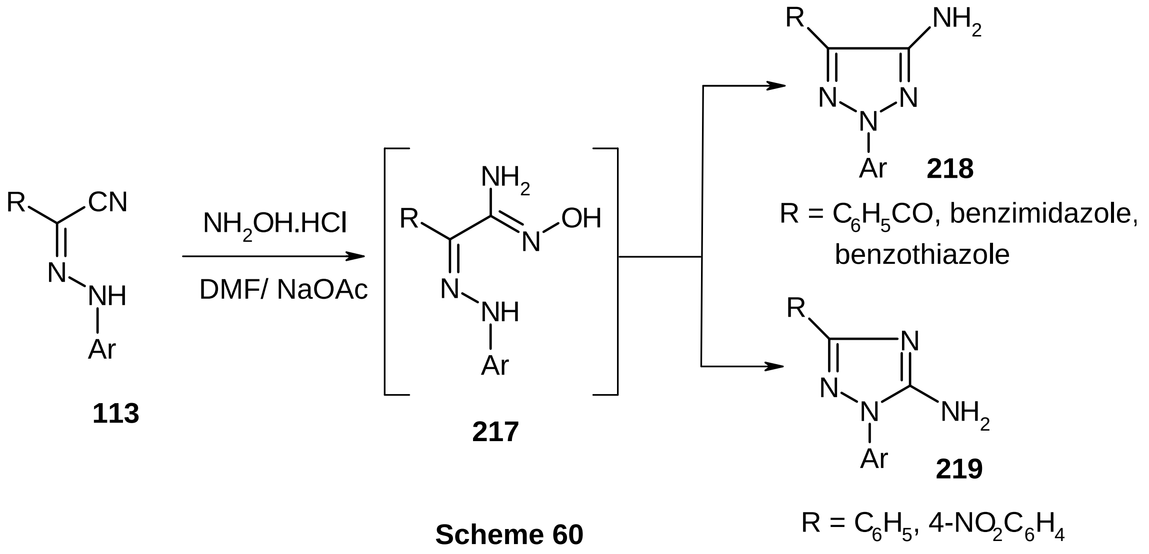
Scheme 58

In contrast to the behavior of **3** the methylarylhydrazones **214** reacted with hydroxylamine hydrochloride and sodium acetate in refluxing ethanol to yield 5-imino-2-isoxazolines **215** which were converted into 4-methylarylhydrazino-3-phenyl-2-isoxazolin-5-one **216** by the action of acetic acid / hydrochloric acid mixture[173] (cf. Scheme 59).



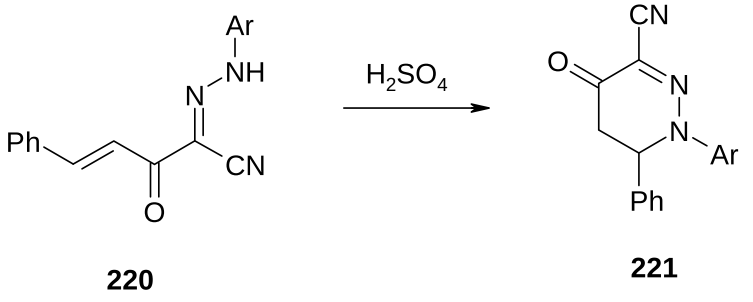
Scheme 59

Arylhydrazono nitriles **113** react with hydroxylamine hydrochloride in dimethyl formamide in presence of sodium acetate to yield amidoximes **217** that cyclized into 1,2,3-triazol-5-amines **218**[174] or 1,2,4-triazol-5-amines **219**[175] depending on the nature of the substituents on hydrazone linkage. The structures of 1,2,3-triazol-5-amine and 1,2,4-triazol-5-amine were established by X-ray crystal structure (cf. Scheme 60).



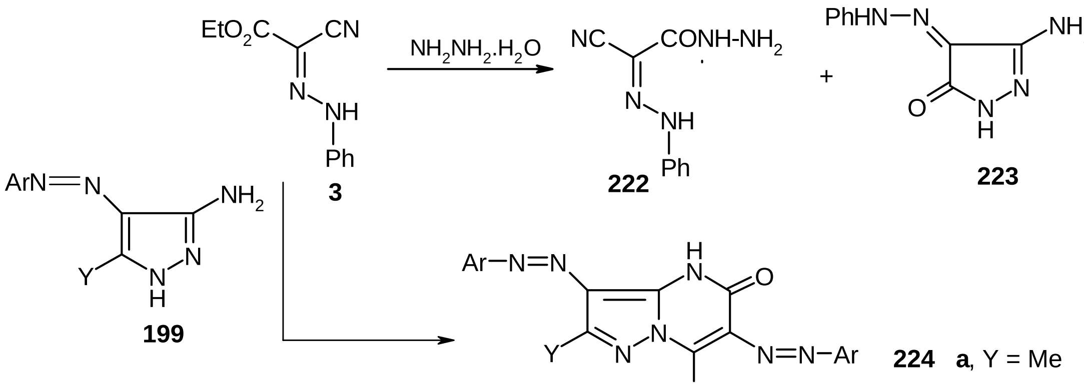
Scheme 60

3-Oxo-5-phenyl-2-(arylhydrazono)-4-pentenenitrile **220** undergoes intramolecular addition reaction to produce the corresponding arylazopyridazine derivatives **221**[176] (cf. Scheme 61).



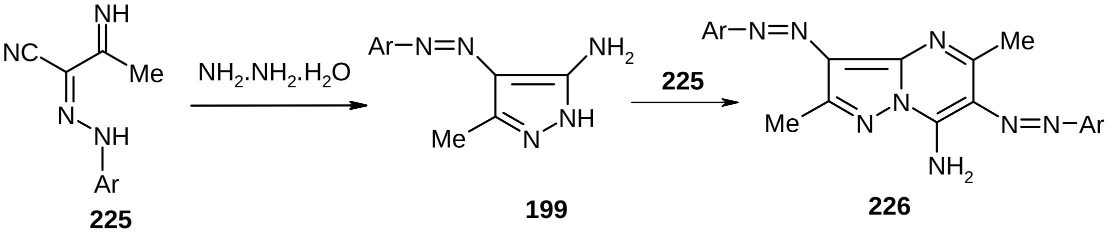
Scheme 61

Ethyl phenylazocyanoacetate **3** reacts with hydrazine hydrate to afford the hydrazide **222** contaminated with 3-amino-4-phenylazo-2-pyrazolin-5-one **223**.[22] Also compound **3** reacted with aminopyrazoles **199** to give pyrazolo[2,3-*a*]pyrimidin-5(4H)-ones **224**[170] (cf. Scheme 62).



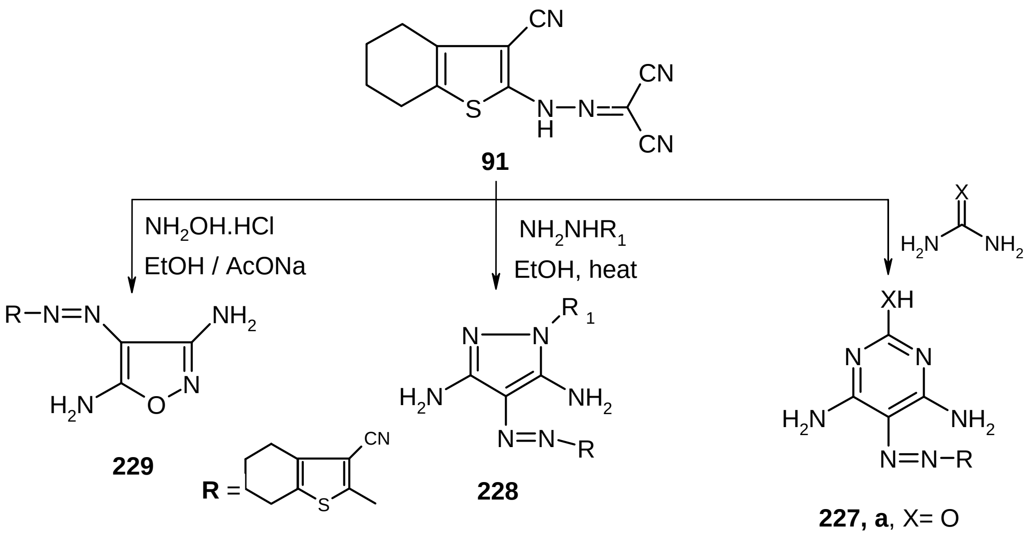
Scheme 62

In a similar manner 2-arylhydrazono-3-ketiminobutyronitriles **225** react with hydrazine hydrate in ethanol to afford 5-amino-4-arylazo-3-methyl-1*H*-pyrazoles **199**. In the presence of excess 2-arylhydrazono-3-ketiminobutyronitriles **225**, the corresponding pyrazolo[2,3-*a*]pyrimidine derivatives **226**[170] were formed (cf. Scheme 63).



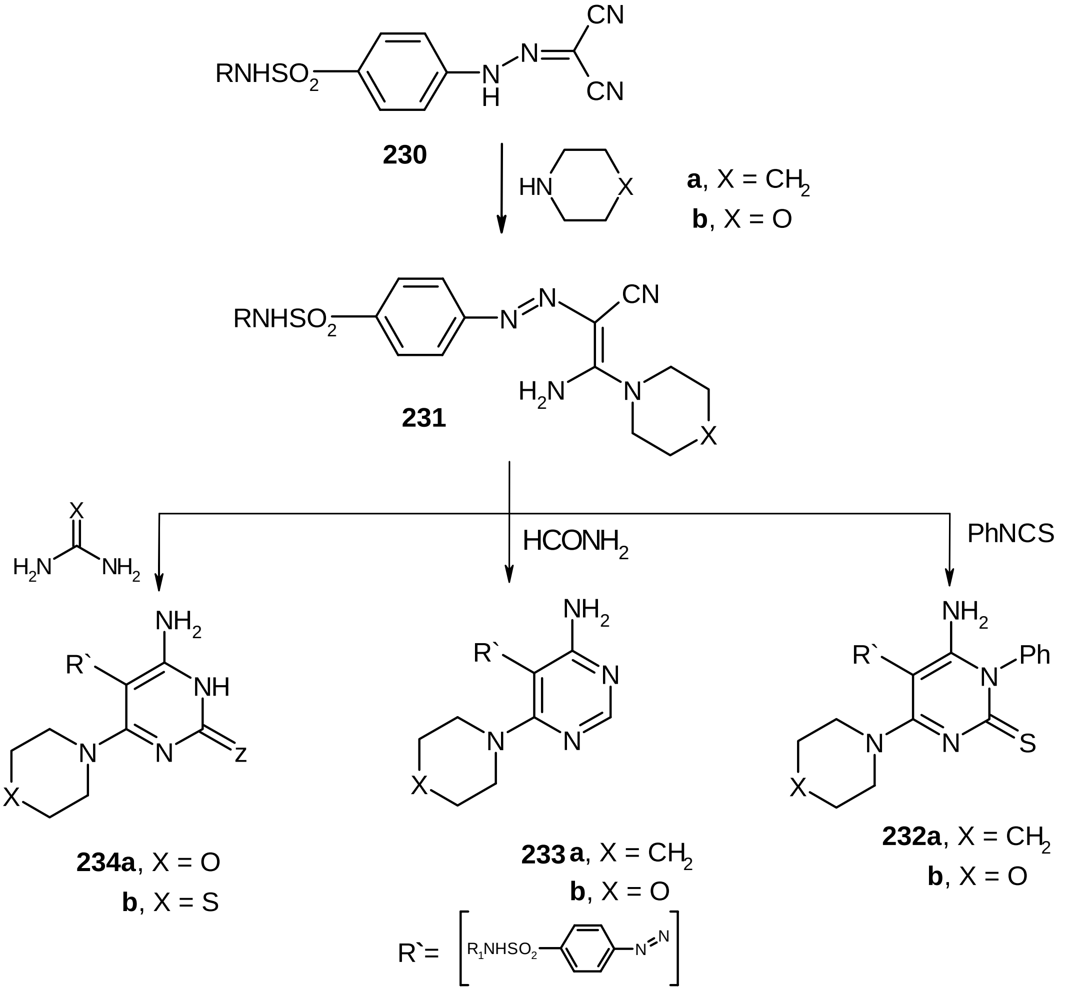
Scheme 63

Reactions of **91** with equimolar proportions of each of urea and thiourea, in ethanolic sodium ethoxide solution provided the corresponding 4,6-diaminopyrimidine derivatives **227a-b** respectively. Also **91** react with hydrazine and hydroxylamine to afford the pyrazole derivatives **228** and the isoxazole derivatives **229** respectively[88] (cf. Scheme 64).



Scheme 64

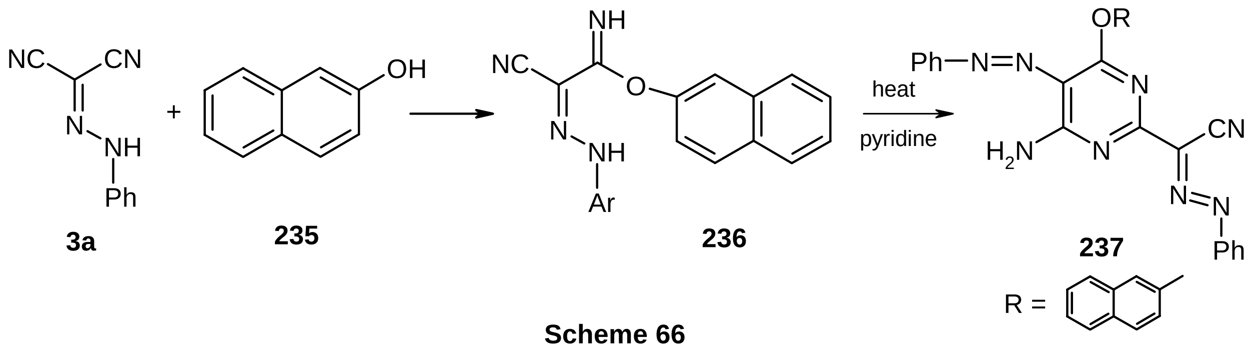
The arylhydrazonomalononitrile derivatives **230** reacted with each of piperidine or morphline respectively to afford the corresponding 1:1 acyclic enaminonitrile adduct **231a-b**. The enaminonitrile moiety in **231** appears to be highly reactive towards nitrogen nucleophiles. Thus compounds **231** reacted with phenylisothiocyanate to afford the corresponding pyrimidinethione derivatives **232**. Similarly condensation of **231** with formamide afforded the aminopyrimidine derivatives **233**. In addition **231** were condensed with urea and thiourea to give **234a-b**[165] (cf. Scheme 65).



Scheme 65

4.3. REACTION WITH OXYGEN NUCLEOPHILES

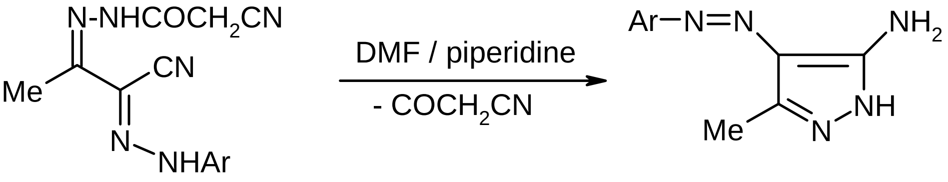
The arylhydrazonomesoxalonitrile **3a** reacts with *β*-naphthol **235** to afford the imine **236** which upon boiling in pyridine affords the pyrimidine derivatives **237**[177] (cf. Scheme 66).



Scheme 66

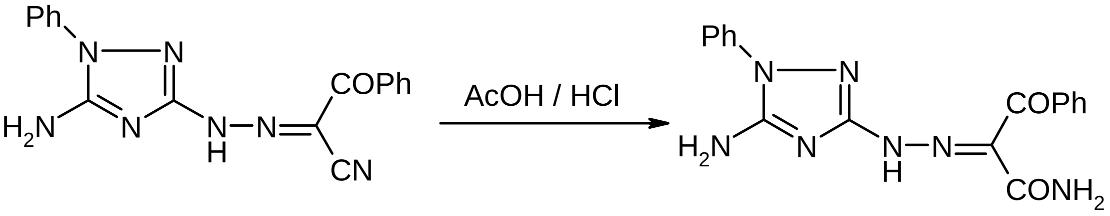
4.4. MISCELLANEOUS REACTIONS

When the hydrazone derivatives **100** was refluxed in DMF / piperidine it was converted into the pyrazole derivatives **199**[92] (cf. Scheme 67).



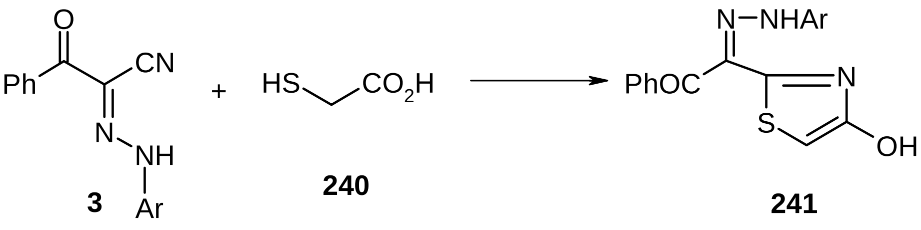
Scheme 67

Attempted cyclization of the hydrazone **238** by the action of acetic acid–hydrochloric acid mixture has resulted in the formation of the amide **239**[84] (cf. Scheme 68).



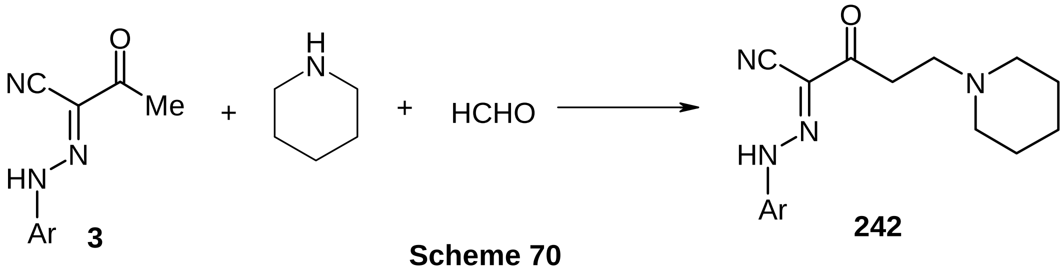
Scheme 68

The arylhydrazonoalkane nitrile **3** reacts with mercaptoacetic acid **240** to afford the corresponding substituted hydroxythiazole **241**[178] (cf. Scheme 69).



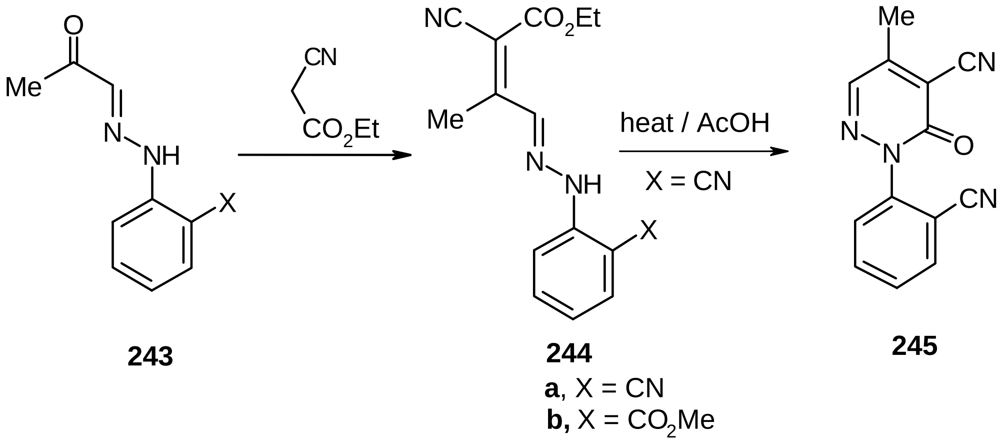
Scheme 69

Arylhydrazonoalkane nitrile **3** reacts with formaldehyde and piperidine to give the corresponding Mannich product **242**[152] (cf. Scheme 70).



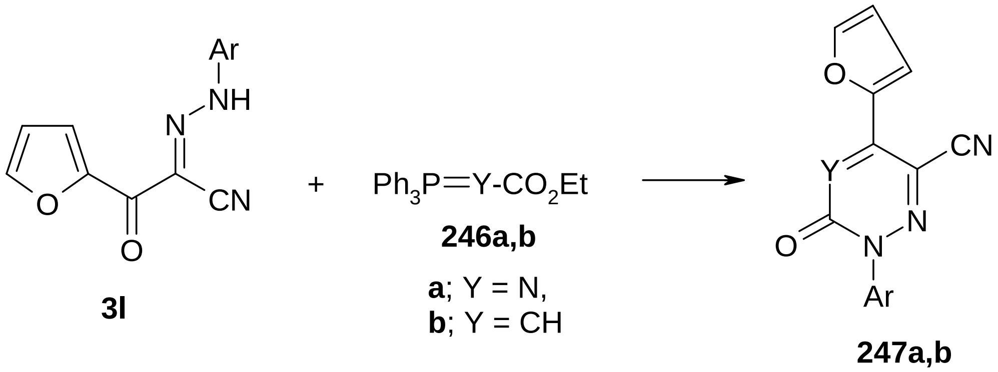
Scheme 70

The azaenamine **243** condensed with ethyl cyanoacetate to afford the corresponding hydrazone **244** which upon reflux in acetic acid for long time afford the pyridazine derivative **245**[174] (cf. Scheme 71).



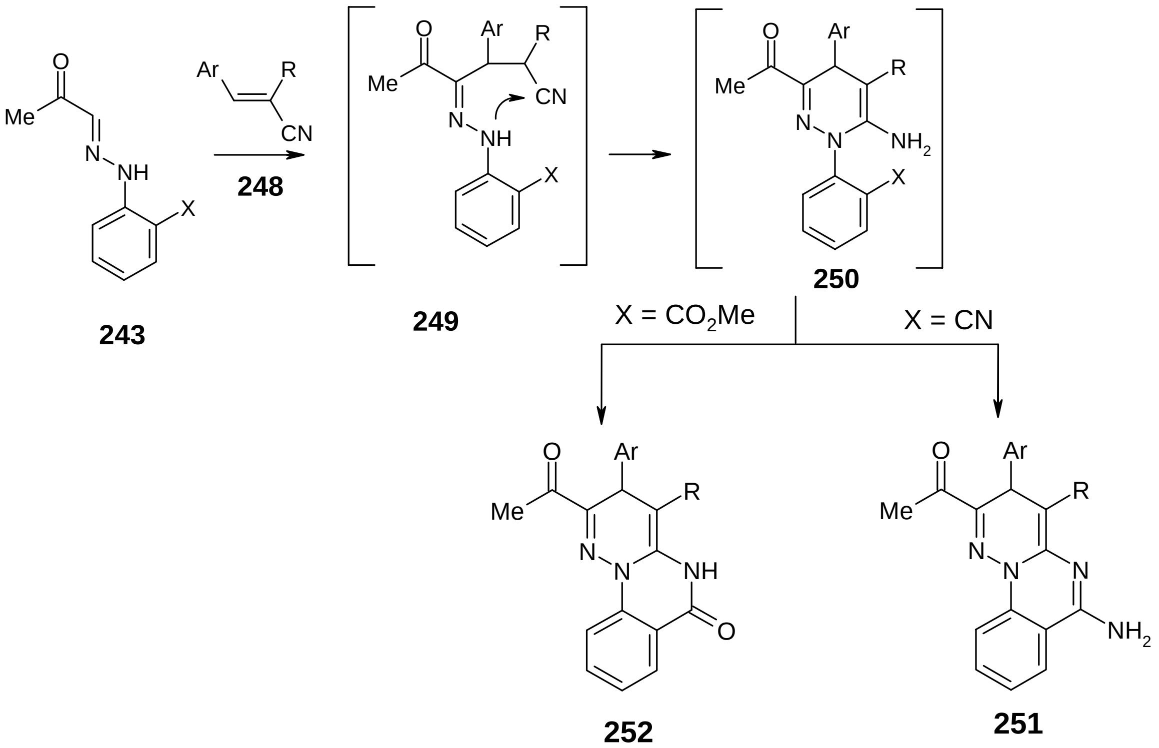
Scheme 71

3-(2-Furyl)-3-oxo-propanenitrile **3l** reacts with some phosphorus ylides **246** to afford 1,2,4-triazine derivatives **247**[32] (cf. Scheme 72).



Scheme 72

Recently it was found that addition of pyruvaldehyde arylhydrazones **243** to α-substituted cinnamonitriles **248**, yielding acyclic **249** which then cyclised into **251** or **252** through intermediate of **250** depending on the substituent[174] (cf. Scheme 73).



Scheme 73

CONCLUSION

We have demonstrated general approach for synthesis of hydrazonoakane nitriles from common building blocks, such as active methylene compounds having cyano group, enaminonitriles, hydrazonoyl halides and oxoalkane nitriles. These hydrazononitriles were used as precursors for synthesis of a variety of azoles, azines and azoloazines compounds.

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REFERENCES

1. M. Parmerter “*Organic Reactions*” Vol. **10** Chapter **1**, ed. by R. Adams, Wiley, New York, N. Y., 1959, p. 4.
2. S. Al-Mousawi, A. Z. Elassar, and M. A. El-Apasery, *Phosphorus, Sulfur, Silicon Relat. Elem.*, 2006, **181**, 1755.
3. M. H. Elnagdi and S. O. Abdallah, *J. prakt. Chem.*, 1973, **315**, 1009.
4. M. S. A. El-Gaby, A. A. Atalla, A. M. Gaber, and K. A. Abd Al-Wahab, *Farmaco,* 2000, **55**, 596.
5. (a) M. H. Elnagdi, M. M. M. Sallam, H. M. Fahmy, S. A. M. Ibrahim, and M. A. M. Elias, *Helv. Chem. Acta*, 1976, **59**, 551. (b) D. S. Brown, J. V. Jollimore, M. P. Merrin, K. Vaughan, and D. L. Hooper, *Can. J. Chem.*, 1995, **73**, 169.

6. M. H. Elnagdi, N. A. L. Kassab, M. E. E. Sobhy, M. R. H. Elmoghayer, and M. U. Wahby, *J. prakt. Chem.*, 1972, **314**, 815.
7. M. H. Elnagdi, M. R. H. Elmoghayer, and D. H. Fleita, *J. prakt. Chem.*, 1974, **316**, 975.
8. H. M. Sammour, H. M. Fahmy, and M. H. Elnagdi, *J. prakt. Chem.*, 1975, **317**, 257.
9. R. M. Mohareb, S. M. Sherif, H. M. Gaber, S. S. Ghabrial, and S. I. Aziz, *Heteroatom. Chem.*, 2004, **15**, 15.
10. P. C. Tsai and I. J. Wang, *Dyes and Pigments*, 2005, **64**, 259.
11. C. Junji and K. Hiroyuki, *Jpn. Pat.*, 1991, 03 143686 (*Chem. Abstr.,* 1992, **116**, 22879j).
12. F. M. Abdel Galil, F. A. Khalifa, and T. S. Abdin, *Dyes and Pigments*, 1990, **12**, 49.
13. D. D. Agarwal and V. Agarwal, *J. Indian Chem. Soc.*, 1991, **68,** 360.
14. N. V. Maatschappij, *Neth. Appl.* 6,411,189, 1965, March 29 (*Chem. Abstr.,* 1965, **63**, 13278b).
15. J. H. Tian and I. J. Wang, *Dyes and Pigments*, 1995, **29**, 181.
16. H. Schmidtmann, *Ber. dtsch. Chem. Ges.,* 1896, **29**, 1168.
17. K. Elbs and H. Lerch, *J. prakt. Chem.*, 1901, **93**, 1.
18. R. E. Kitson and N. E. Griffith, *Anal. Chem.,* 1952, **24**, 334.
19. E. V. Meyer, *J. prakt. Chem.*, 1895, **52**, 81.
20. A. S. Shawali and M. Abd-Galil, *Tetrahedron*, 1971, **27**, 4305.
21. A. M. Negm, F. M. Abdelrazek, M. H. Elnagdi, and L. H. Shaaban, *Arch. Pharmacol. Res.,* 1994, **17**, 411.
22. E. M. Kandeel, K. U. Sadek, and M. H. Elnagdi, *Z. Naturforsch,* 1980, **35b**, 91.
23. L. Legradi, *Talanta*, 1970, **17**, 161.
24. H. Schafer and K. Gewald, *J. prakt. Chem.,* 1974, **316**, 684.
25. H. F. Zohdi, N. M. Rateb, and A. O. Abdelhamid, *Phosphorus, Sulfur, Silicon Relat. Elem.*, 1998, **133**, 103.
26. A. O. Abdelhamid and S. E. Abdou, *Sulfur Lett*., 1987, **6**, 41.
27. H. Z. Shams, F. A. Khalifa, B. N. Barsoum, and M. M. Naoum, *Bull. Soc. Chim. Fr.,* 1989, 119.
28. S. A. Mansour, W. M. Eldeib, S. E. Abdou, and H. A. Daboun, *Sulfur Lett.,* 1987, **6**, 181.
29. M. H. Elnagdi, M. R. H. Elmoghayer, A. E. G. Hammam, and S. A. Khallaf, *J. Heterocycl. Chem.,* 1979, **16**, 1541.
30. M. R. H. Elmoghayer, E. A. Ghali, M. M. M. Ramiz, and M. H. Elnagdi, *Liebigs Ann. Chem.,* 1985, 1962.
31. A. G. A. El-Agamey, I. El-Sakka, Z. El-Shahat, and M. H. Elnagdi, *Arch. Pharm. (Weinheim),* 1984, **317***,* 289.
32. A. M. Farag, K. M. Dawood, and H. A. Abdel-Aziz, *J. Chem. Res. (S),* 2004, 808.
33. F. M. Abdel Galil and M. H. Elnagdi, *Liebigs Ann. Chem.,* 1987, 477.
34. M. M. Abdel-Khalik, M. H. Elnagdi, and S. M. Agamy, *Synthesis,* 2000, 1166.
35. M. I. Rudnev, V. P. Kurbatov, N. K. Chub, and O. A. Osipov, *Zh. Org. Khim.*, 1988, **58**, 2334.
36. R. G. Dubenko, I. M. Bazavova, and E. F. Gorbenko, *Zh. Org. Khim.*, 1984, **20**, 577.
37. S. M. Rida, F. A. Ashour, S. A. M. El-Hawash, M. M. ElSemary, M. H. Badr, and M. A. Shalaby, *Eur. J. Med. Chem*., 2005, **40**, 949.
38. F. Al-Omran, N. Al-Awadi, O. Yousef, and M. H. Elnagdi, *J. Heterocycl. Chem.*, 2000, **37**, 167.
39. T. L. Cupps, D. S. Wise, and L. B. Townsend, *J. Org. Chem.*, 1982, **47**, 5115.
40. N. S. Ibrahim, F. M. Abdel-Galil, R. M. Abdel-Motaleb, and M. H. Elnagdi, *Bull. Chem. Soc. Jpn.,* 1987, **60**, 4486.
41. N. S. Ibrahim, F. M. Abdel-Galil, R. M. Abdel-Motaleb, and M. H. Elnagdi, *Heterocycles,* 1986, **24**, 1219.
42. M. Coenen, *Justus Liebigs Ann. Chem.,* 1961, **85**, 640.
43. E. A. A. Hafez, Z. E. Kandeel, and M. H. Elnagdi, *J. Heterocycl. Chem*., 1987, **24**, 227.
44. S. El-Kousy, I. El-Sakka, A. M. El-Torgoman, H. Roshdy, and M. H. Elnagdi, *Collect. Czech. Chem. Commun.,* 1990, **55**, 2977.

45. M. H. Elnagdi, F. A. M. Abdel Aal, E. A. A. Hafez, and Y. M. Yassin, *Z. Naturforsch.,* 1989, **44b**, 683.

46. G. E. H. Elgemeie, H. A. Elfahham, and M. H. Elnagdi, *Heterocycles,* 1985, **23**, 1999.

47. S. Al-Mousawi, K. S. George, and M. H. Elnagdi, *Pharmazie*, 1999, **54**, 571.

48. S. M. Fahmy, N. M. Abed, R. M. Mohareb, and M. H. Elnagdi, *Synthesis,* 1982, 490.

49. A. M. A. Helmy, M. A. Morsi, and M. H. Elnagdi, *Collect. Czech. Chem. Commun.,* 1994, **59**, 1752.

50. M. H. Elnagdi, K. U. Sadek, N. M. Taha, and Y. M. Yassin, *Collect. Czech. Chem. Commun.,* 1990, **55**, 734.

51. E. A. A. Hafez, M. A. E. Khalifa, S. K. A. Guda, and M. H. Elnagdi, *Z. Naturforsch.,* 1980, **35b**, 485.

52. K. U. Sadek, S. M. Fahmy, R. M. Mohareb, and M. H. Elnagdi, *J. Chem. Eng. Data,* 1984, **29**, 101.

53. N. M. Abed, N. S. Ibrahim, S. M. Fahmy, and M. H. Elnagdi, *Org. Prep. Proced. Int.,* 1985, **17**, 107.

54. A. O. Abdelhamid, N. M. Abed, and A. M. Farag, *Quim. Org. Bioquim.,* 1988, **84**, 22.

55. Z. E. Kandeel, F. M. Abdelrazek, M. H. Elnagdi, and A. El-Torgeman, *Heterocycles,* 1986, **24,** 2455.

56. M. H. Mohamed, N. S. Ibrahim, and M. H. Elnagdi, *Heterocycles,* 1987, **26**, 899.

57. M. H. Elnagdi, H. A. Elfahham, and G. E. H. Elgemeie, *Heterocycles,* 1983, **20,** 519.

58. K. Gewald and U. Hain, *Synthesis,* 1984, 62.

59. A. Z. A. Elassar, Y. M. Elkholy, and M. H. Elnagdi, *J. prakt. Chem*., 1998, **340**, 491.

60. M. Mittelbach, U. Wagner, and C. Kratky, *Liebigs Ann. Chem.,* 1987, 889.

61. H. Junek, G. Uray, and A. Kotzent, *Monatsh. Chem*., 1983, **114**, 973.

62. F. M. Manhi, S. E. Zayed, F. A. Ali, and M. H. Elnagdi, *Collect. Czech. Chem. Commun.,* 1992, **57**, 1770.

63. F. A. Attaby and S. M. Eldin, *Phosphorus, Sulfur Silicon Relat. Elem.,* 1991, **56**, 59.

64. F. M. Abdelrazek, A. M. S. El-Din, and A. E. Mekky, *Tetrahedron,* 2001, **57**, 1813.

65. M. H. Elnagdi, M. R. H. Elmoghayer, S. M. Fahmy, M. K. A. Ibraheim, and H. H. Alnima, *Z. Naturforsch.,* 1978, **33b**, 216.

66. R. J. Kobylecki and A. Mckillop, "*Advances Heterocyclic Chemistry,*" Vol. **19**, ed. by A. R. Katritzky and A. J. Boultion, 1976, p. 25.

67. M. H. Elnagdi, E. M. Zayed, and S. M. Abdou, *Heterocycles,* 1982, **19**, 559.

68. H. Mackie and G. Tennant, *Tetrahedron Lett.,* 1972, **13**, 4719.

69. M. H. Elnagdi, M. R. H. Elmoghayer, D. H. Fleita, E. A. A. Hafez, and S. M. Fahmy, *J. Org. Chem*., 1976, **41**, 3781.

70. M. H. Elnagdi, M. R. H. Elmoghayer, E. M. Kandeel, and M. K. A. Ibraheim, *J. Heterocycl. Chem.,* 1977, **14**, 227.

71. J. Slouka, J. Kubata, and V. Bekarek, *Acta. Univ. Palacki. Olomuc. Fac. Rerum Nat.*, 1976, **49**, 219 (*Chem. Abstr.,* 1977, **87**, 68291x).

72. F. M. Abdel-Galil, S. M. Sherif, and M. H. Elnagdi, *Heterocycles,* 1986, **24**, 2023.

73. H. A. Elfahham, G. E. H. Elgemeie, Y. R. Ibraheim, and M. H. Elnagdi, *Liebigs Ann. Chem.,* 1988, 819.

74. K. U. Sadek, M. A. Selim, M. H. Elnagdi, and H. H. Otto, *Bull. Chem. Soc. Jpn.,* 1993, **66**, 2927.

75. M. H. Elnagdi, E. M. Zayed, M. A. E. Khalifa, and S. A. Ghozlan, *Monatsh. Chem*., 1981, **112**, 245.

76. T. M. Abu Elmaati and F. M. El Taweel, *J. Heterocycl. Chem.,* 2004, **41**, 109.

77. M. A. Raslan, R. M. Abd El-Aal, M. E. Hassan, N. A. Ahmed, and K. U. Sadek, *J. Chin. Chem. Soc.,* 2001, **48**, 91.

78. O. A. Fathalla and M. E. Zaki, *Indian J. Chem.,* 1998, **37B**, 484.

79. A. M. Farag, K. M. Dawood, and Z. E. Kandeel, *Tetrahedron,* 1996, **52**, 7893.

80. A. M. Farag, *J. Chem. Res. (S),* 1994, 432.
81. M. A. Morsi, H. M. Fahmy, M. H. Elnagdi, and M. M. Azzam, *Rev. Port. Quit.*, 1981, **23**, 37.
82. F. A. El-Saied, M. I. Ayad, R. M. Issa, and S. A. Aly, *Polish J. Chem.*, 2000, **74**, 91.
83. E. M. Zayed, M. A. E. Khalifa, L. I. Ibraheim, and M. H. Elnagdi, *Arch. Pharm. (Weinheim),* 1983, **316**, 105.
84. E. A. A. Hafez, N. M. Abed, I. A. Elsaka, and M. H. Elnagdi, *J. Heterocycl. Chem.,* 1983, **20**, 285.
85. K. M. Dawood, A. M. Farag, E. A. Ragab, and Z. E. Kandeel, *J. Chem. Res. (S),* 2000, 206.
86. Y. W. Ho, *Dyes and Pigments*, 2005, **64**, 223.
87. S. M. Sherif, W. W. Wardakhan, and R. M. Mohareb, *J. Chem. Res. (S)*, 1996, 356.
88. S. M. Sherif, R. M. Mohareb, H. Z. Shams, and H. M. M. Gaber, *J. Chem. Res. (S),* 1995, 434.
89. R. W. Sabnis and D. W. Rangnekar, *Dyes and Pigments*, 1989, **10**, 295.
90. P. Winternitz, *Helv. Chim. Acta*, 1978, **61**, 1175.
91. H. F. Anwar, D. H. Fleita, H. Kolshorn, H. Meier, and M. H. Elnagdi, *ARKIVOC*, 2006, **xv**, 133.
92. A. W. Erian, S. I. Aziz, A. M. Negm, and S. M. Sherif, *J. Chem. Res. (S)*, 1993, 352.
93. I. S. A. Hafiz, *Z. Naturforsch.,* 2000, **55b**, 321.
94. F. Al-Omran, M. M. Abdel-Khalik, A. Abou-Elkhair, and M. H. Elnagdi, *Synthesis,* 1997, 91.
95. S. A. S. Ghozlan, I. A. Abdelhamid, H. M. Gaber, and M. H. Elnagdi, *J. Chem. Res. (S),* 2004, 789.
96. S. O. Abdallah, N. H. Metwally, H. F. Anwar, and M. H. Elnagdi, *J. Heterocycl. Chem*., 2005, **42**, 781.
97. A. A. Abbas and A. H. M. Elwahy, *Synthesis,* 2001, 1331.
98. M. M. Abdel-Khalik, S. M. Agamy, and M. H. Elnagdi, *Z. Naturforsch.,* 2000, **55b**, 1211.
99. A. S. Shawali, M. H. Abdelkader, and F. M. A. Eltalbawy, *Tetrahedron,* 2002, **58**, 2875.
100. A. S. Shawali and A. O. Abdelhamid, *Bull. Chem. Soc. Jpn.,* 1976, **49**, 321.
101. C. Parkanyi and A. S. Shawali, *J. Heterocycl. Chem*., 1980, **17**, 897.
102. H. P. Kaufmann and L. S. Huang, *Chem. Ber*., 1942, **75**, 1214.
103. A. O. Abdelhamid, *Phosphorus, Sulfur and Silicon,* 1994, **88**, 217.
104. B. Al-Saleh, M. A. El-Apasery, and M. H. Elnagdi, *J. Chem. Res. (S)*, 2004, 578.
105. M. A. Al-Shiekh, A. M. Salah El-Din, E. A. Hafez, and M. H. Elnagdi, *J. Heterocycl. Chem*., 2004, **41**, 647.
106. H. Behbehani, M. M. Abdel-Khalik, and M. H. Elnagdi, *Org. Prep. Proced. Int.,*1999, **31**, 551.
107. K. M. Al-Zaydi, *J. Saudi Chem. Soc.*, 2002, **6**, 477.
108. K. M. Al-Zaydi, R. M. Borik, and M. H. Elnagdi, *Molecules*, 2003, **8**, 910.
109. M. Jachak, U. Kriessmann, M. Mittelbach, and H. Junek, *Monatsh. Chem*., 1993, **124**, 199.
110. E. A. A. Hafez, N. M. Abed, M. R. H. Elmoghayer, and A. G. A. El-Agamey, *Heterocycles,* 1984, **22**, 1821.
111. S. P. Watson, R. D. Wilson, D. B. Judd, and S. A. Richards, *Tetrahedron,* 1997, **38**, 9065.
112. D. E. Tupper and M. R. Bray, *Synthesis,* 1997, 337.
113. R. D. Wilson, S. P. Watson, and S. A. Richards, *Tetrahedron Lett.,* 1998, **39**, 2827.
114. S. Cusmano and V. Sprio, *Gazz. Chim. Ital*., 1952, **82**, 373.
115. V. Sprio and I. Fabra, *Atti Accad. Sci. Lett. Arti Palermo*, 1972, **31**, 173 (*Chem Abstr.,* 1973, **79**, 105185y).
116. S. Cusmano and V. Sprio, *Gazz. Chim. Ital*., 1952, **82**, 191.
117. S. Cusmano and V. Sprio, *Gazz. Chim. Ital*., 1952, **82**, 420.
118. M. H. Elnagdi, M. A. E. Khalifa, M. K. A. Ibrahim, and M. R. H. Elmoghayer, *J. Heterocycl. Chem.,* 1981, **18**, 877.
119. S. Kamba, K. Saito, A. Sakurai, and H. Midorikawa, *Synthesis,* 1980, 839.
120. M. H. Elnagdi, D. H. Fleita, and M. R. H. Elmoghayer, *Tetrahedron,* 1975, **31**, 63.
121. M. H. Elnagdi, M. R. H. Elmoghayer, H. A. Elfahham, M. M. Sallam, and H. H. Alnima, *J. Heterocycl. Chem.,* 1980, **17**, 209.

122. M. H. Elnagdi, E. A. A. Hafez, H. A. Elfahham, and E. M. Kandeel, *J. Heterocycl. Chem.,* 1980, **17**, 73.
123. M. K. A. Ibrahim and K. U. Sadek, *Polish J. Chem.,* 1983, **57**, 153.
124. M. H. Elnagdi, H. M. Fahmy, and M. A. Morsi, *J. Electroanal. Chem. Interfacial Electrochem.*, 1976, **68**, 237.
125. M. H. Elnagdi and H. M. Fahmy, *J. Electroanal. Chem. Interfacial Electrochem.*, 1977, **84**, 149.
126. M. A. Morsi, A. M. Helmy, and H. M. Fahmy, *J. Electroanal. Chem. Interfacial Electrochem.*, 1983, **148**, 123.
127. H. M. Fahmy and M. H. Elnagdi, *Electrochim. Acta*, 1978, **23**, 255.
128. M. A. Morsi, E. M. Zayed, L. I. Ibrahim, and M. H. Elnagdi, *Ann. Chem. (Italy)*, 1983, **73**, 213.
129. M. A. Morsi, H. M. Fahmy, M. H. Elnagdi, and M. Abdel Azzem, *J. Electroanal. Chem. Interfacial Electrochem.*, 1982, **133**, 269.
130. G. M. Abou-Elenien, N. A. Ismail, M. M. Hassanin, and A. A. Fahmy, *Can. J. Chem.*, 1992, **70**, 2704.
131. G. Cauquis, H. M. Fahmy, G. Pierre, and Z. E. Kandeel, *J. Electroanal. Chem. Interfacial Electrochem.*, 1981, **124**, 133.
132. G. M. Abou-Elenien, N. A. Ismail, and T. S. Hafez, *Bull. Chem. Soc. Jpn.,* 1991, **64**, 651.
133. A. S. Perlin, *Can. J. Chem./Rev. Can. Chim.*, 1966, **44**, 539.
134. S. I. Aziz, H. F. Anwar, D. H. Felita, and M. H. Elnagdi, *J. Heterocycl. Chem.*, 2007, **44**, 727.
135. O. M. E. El-Dusouqui, M. M. Abdelkhalik, N. A. Al-Awadi, H. H. Dib, B. J. George, and M. H. Elnagdi, *J. Chem. Res.,* 2006, 295.
136. I. M. Kenawi and M. H. Elnagdi, *Spectrochim. Acta Molecul. Biomolecul. Spectroscopy,* 2006, **65A**, 805; E. H. Hafez and M. H. Elnagdi, unpublished data.
137. M. H. Elnagdi, E. M. Zayed, S. M. Fahmy, M. A. G. Khalifa, and S. Amir, *Gazz. Chim. Ital.*, 1977, **107**, 555.
138. M. S. T. Goncalves, A. M. F. Oliveira-Campos, L. M. Rodrigues, M. F. R. P. Proenca, J. Griffiths, H. L. S. Maia, M. Kaja, and R. Hrdina, *J. Chem. Res*., 2004, 115.
139. K. Gewald, O. Calderon, H. Schaefer, and U. Hain, *Liebigs Ann. Chem.*, 1984, 1390.
140. A. M. Amer, M. M. El-Mobayed, and S. Asker, *Monatsh. Chem.*, 2004, **135**, 595.
141. J. C. V. P. Moura, A. M. F. Oliveira-Campos, J. Griffiths, H. L. S. Maia, and J. I. N. R. Gomes, *J. Chem. Res. (S),* 1995, 128.
142. R. Brehme, E. Grundemann, M. Schneider, R. Radeglia, G. Reck, and B. Schulz, *Synthesis,* 2003, 1615.
143. R. Brehme and H. E. Nikolajewski, *Tetrahedron Lett*., 1982, **23**, 1131.
144. R. Brehme and H. E. Nikolajewski, *Tetrahedron*, 1969, **25**, 1159.
145. R. Brehme and H. E. Nikolajewski, *Tetrahedron*, 1976, **32**, 731.
146. R. M. Abdel-Motaleb, A. A. Makhloof, H. M. Ibrahim, and M. H. Elnagdi, *J. Heterocycl. Chem*., 2007, **44**, 109.
147. J. Slouka and M. Budikova, *Acta. Univ. Palacki. Olomuc. Fac. Rerum Nat.*, 1974, **45**, 113 (*Chem. Abstr.,* 1975, **82**, 125360).
148. L. X. Zhao and Q. X. Yao, *Yaoxue Xuebao*, 1991, **25**, 739.
149. R. M. Abdel-Motaleb, A. A. Makhloof, H. M. Ibrahim, and M. H. Elnagdi, *J. Heterocycl. Chem.,* 2006, **43**, 931.
150. A. H. Harhash, A. K. Mansour, M. H. Elnagdi, and M. R. H. Elmoghayer, *J. prakt. Chem.*, 1973, **315**, 235.
151. M. H. Elnagdi, F. M. Abdelrazek, N. S. Ibrahim, and A. W. Erian, *Tetrahedron*, 1989, **45**, 3597.
152. H. M. Bakeer, *J. Indian Chem. Soc*., 1992, **69**, 314.
153. H. M. Bakeer, *J. Serbian Chem. Soc*., 1992, **57**, 725.
154. H. Al-Awadhi, F. Al-Omran, M. H. Elnagdi, L. Infantes, C. Foces-Foces, N. Jagerovic, and J. Elguero, *Tetrahedron*, 1995, **51**, 12745.

155. M. H. Elnagdi, F. A. M. Abdul-Aal, N. M. Taha, and Y. M. Yassin, *Z. Naturforsch.,* 1990, **45b**, 389.
156. L. Grubert, M. Patzel, W. Jugelt, B. Riemer, and J. Liebscher, *Liebigs Ann. Chem.,* 1994, 1005.
157. M. H. Elnagdi, A. M. Negm, and K. U. Sadek, *Synlett*, 1994, 27.
158. A. H. H. Elghandour, M. K. A. Ibrahim, I. S. A. Hafiz, and M. H. Elnagdi, *Org. Prep. Proced. Int.,* 1993, **25**, 293.
159. M. Sako, *Sci. Synthesis*, 2004, **16**, 1109.
160. M. H. Elnagdi, 18th Int. Cogress in Heterocyclic Chem. Graz, Austria, 1981, p. 12, 22.
161. K. Gewald, H. Hain, and M. Gruner, *Chem. Ber.,* 1985, **118**, 2198.
162. S. M. El-Kousy, R. M. Mohareb, M. Riad, and M. H. Elnagdi, *Pakistan J. Sci. Ind. Res.,* 1998, **41**, 81.
163. I. A. El-Sakka, *J. Chem. Res. (S)*, 1996, 434.
164. R. M. Mohareb and N. S. Abdel-Sayed, *Coll. Czech. Chem. Commun.*, 1992, **57**, 1758.
165. A. Z. A. E. Hassanien, I. S. A. Hafiz, and M. H. Elnagdi, *J. Chem. Res. (S)*, 1999, 8.
166. Z. E. Kandeel, *J. Chem. Res. (S)*, 1995, 290.
167. M. M. Abdel-Khalik, *J. Chem. Res. (S)*, 1997, 198.
168. A. M. Negm, F. M. Abdelrazek, M. H. Elnagdi, and L. H. Shaaban, *Egypt. J. Chem.,* 1994, **37**, 509.
169. E. M. Zayed and S. A. S. Ghozlan, *Z. Naturforsch.,* 1985, **40b**, 1727.
170. F. Karci, *Coloration Technology*, 2005, **121**, 275.
171. Y. W. Ho and I. J. Wang, *Dyes and Pigments*, 1995, **29**, 295.
172. P. Cankar, I. Wiedermannova, and J. Slouka, *Chemica.,* 2002, **41**, 7.
173. M. H. Elnagdi, M. R. H. Elmoghayer, E. A. A. Hafez, and H. H. Alnima, *J. Org. Chem.*, 1975, **40**, 2604.
174. S. A. S. Ghozlan, I. A. Abdelhamid, and M. H. Elnagdi, *ARKIVOCK,* 2006, **xiii**, 147.
175. H. M. Al-Matar, S. M. Riyadh, and M. H. Elnagdi, *ARKIVOCK,* 2007, **xiii**, 53.
176. G. A. M. Nawwar, R. H. Swellem, and L. M. Chabaka, *Coll. Czech. Chem. Commun.*, 1994, **59**, 186.
177. M. H. Elnagdi, A. H. H. Elghandour, A. F. A. Harb, A. H. M. Hussien, and S. A. M. Metwally, *Heterocycles,* 1994, **38**, 739.
178. F. M. A. El-Taweel, M. A. H. Mashaly, and A. G. A. Elagamey, *Arch. Pharmacal. Res.*, 1990, **13**, 261.

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