Chemistry of carbofunctionally substituted hydrazones

Abdel-Zaher A. Elassar, Hicham H. Dib, Nouria A. Al-Awadi, and Mohammad H. Elnagdi

Chemistry Department, Faculty of science, Kuwait University, P. O. Box 5969- Safat-13060, Kuwait
E-mail: aelassar@yahoo.com

Abstract
Synthetic approaches and chemical reactivity of title compounds since 1894 to date are reported. Emphasis is placed on pinpointing old literature reports that need reinspection in light of modern techniques and recent advances in utilizing the title compounds as precursors to polyfunctional heteroaromatics.

Keywords: Tautomerism, arylhydrazones as nucleophiles, carbon Mitsunobu reaction, aryl hydrazones as precursors to polyfunctional azoles and azines, gas phase pyrolysis

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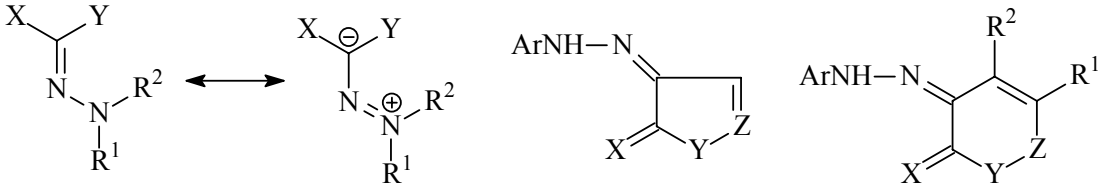
1. Introduction

Hydrazones in which X and Y are carbon functionality as CO_2R, CN are extremely important compounds in dye industry. [1-3] Nitrogen lone pair resonance (cf. Scheme 1) renders hydrazone carbon atom electron rich and nucleophilicity of this carbon atom although have been noted in old literature [4] has now been recognized and utilized extensively in synthesis. Despite their theoretical and practical importance to our knowledge, no trial to review reported chemical reactivities, structural studies and synthetic approaches to those molecules has ever been made. In the following article we review the chemistry of this class of compounds. Arylhydrazono azoles, azines and their condensed derivatives if having an α-functional group on ring nitrogen (e.g. **3** and or **4**) are not considered in this review as plenty of these derivatives have been extensively utilized as dyes and their chemistry is reviewed in specialized dye chemistry texts[3]. The chemistry of hydrazonyl halide X or Y = halogen and of hydrazononitriles X or Y = CN have been surveyed recently and will not be included here.



1 **2** **3** **4**

Scheme 1

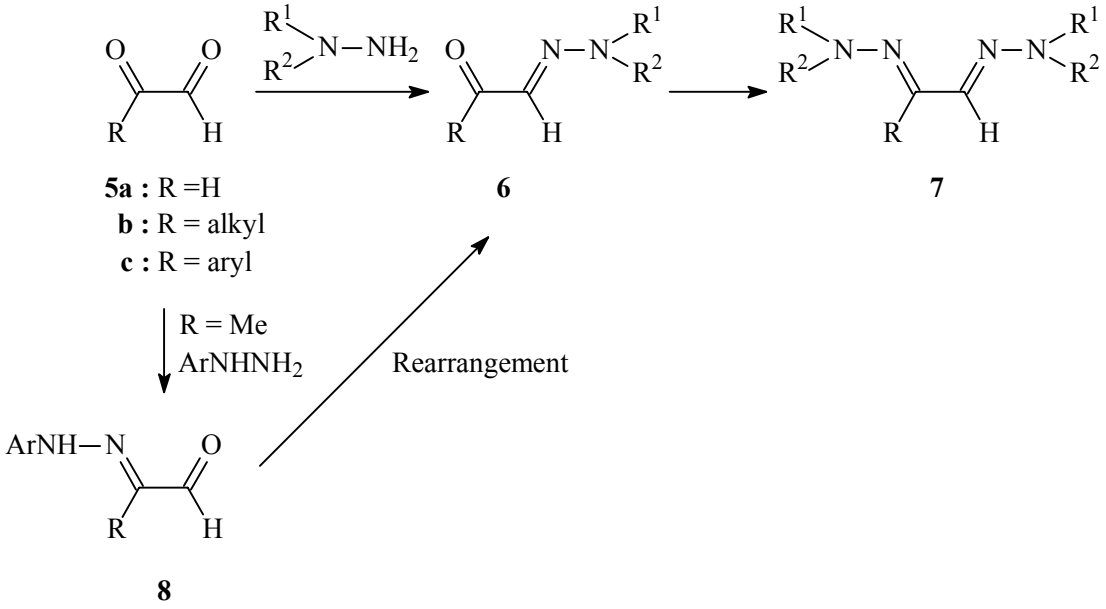
2. Synthetic Approaches to Carbofunctionally Substituted Hydrazones

2.1. Condensation of functionalized aldehydes and ketones with hydrazines

This is a most logical route provided the required α-functional aldehyde and / or ketone is easily obtainable. As functionally substituted aldehydes are generally difficult to obtain and store this route however has only relatively limited application for the synthesis of monofunctionally substituted hydrazone [5-11]

Condensing glyoxal **5a** and substituted glyoxal **5b,c** with substituted hydrazines leads to formation of mono or bis hydrazones **6** or **7** depending on molar ratio and applied reaction

conditions[5-11] It has been reported that **5b** reacts with phenylhydrazine to yield initially **8** which then rearranges into the thermodynamically stable **6**; R = CH_3 (cf. Scheme 2). The mechanism of this rearrangement however had to be classified although reversibility of initial condensation reaction might be visional and that 8 is the kinetic product.

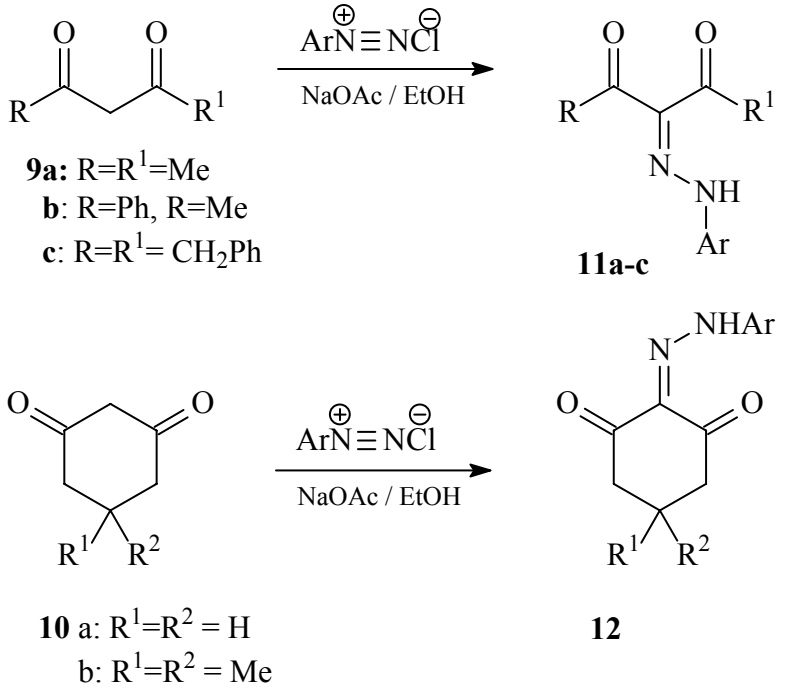


Scheme 2

2.2. Coupling active methylenes with aromatic and heteroaromatic diazonium salts

This is the most generally utilized route to **1**. The coupling reaction is generally conducted at room temperature and in protic organic solvent in presence of a base. Sodium acetate is most commonly used but coupling in presence of sodium hydroxide or in pyridine solutions has been reported.

Acetylacetone **9a**, benzoylacetone **9b**, diphenylpentanedione **9c** and other 1,3-diketones including cyclic ketones (e.g. **10a,b**) have been coupled with aromatic diazonium salts in ethanolic sodium acetate to yield corresponding coupling products **11a-c** [12-20] and **12a,b** [21,22] (cf. Scheme 3).



9a: R=R^1=Me
b: R=Ph, R=Me
c: R=R^1= CH_2Ph

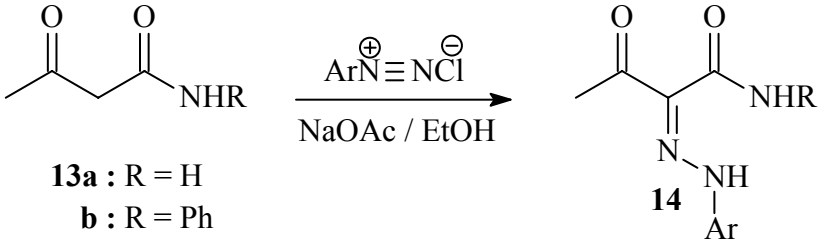
11a-c

10 a: R^1=R^2 = H
b: R^1=R^2 = Me

12

Scheme 3

Similarly, oxobutanamide **13a** and oxophenylbutanamide **13b** couple readily to yield aryl hydrazones **14a,b**[23-34] that have been extensively used as dyes and pigments (cf. Scheme 4).

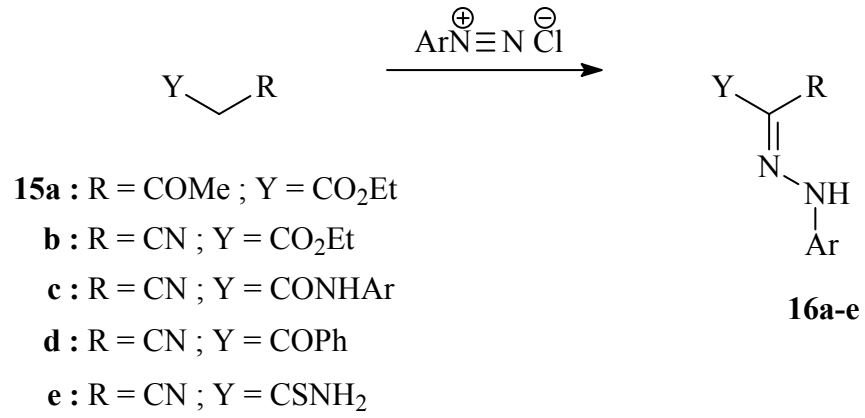


13a : R = H
b : R = Ph

14

Scheme 4

Ethyl acetoacetate **15a**[35-50] ethyl cyanoacetate **15b**,[51-66] cyanoanilides **15c**,[67-69] benzoylacetonitrile **15d**[70] and cyanothioacetamide **15f**[71,72] couple readily with aromatic diazonium salt in presence of sodium acetate to yield corresponding arylhydrazones whose exact geometry has only been recently established **16** (cf. Scheme 5).



15a : R = COMe ; Y = CO_2Et

b : R = CN ; Y = CO_2Et

c : R = CN ; Y = CONHAr

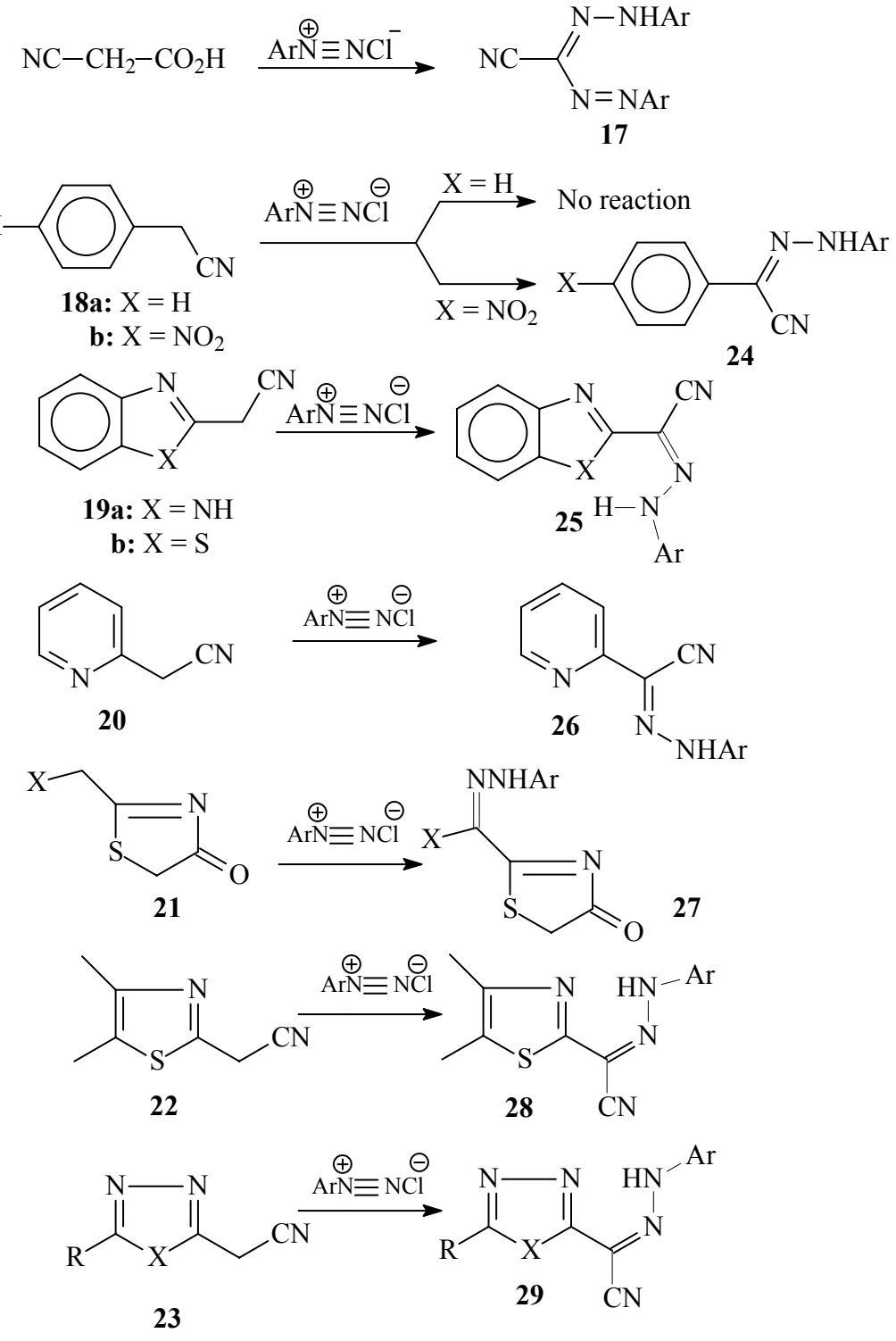
d : R = CN ; Y = COPh

e : R = CN ; Y = $CSNH_2$

16a-e

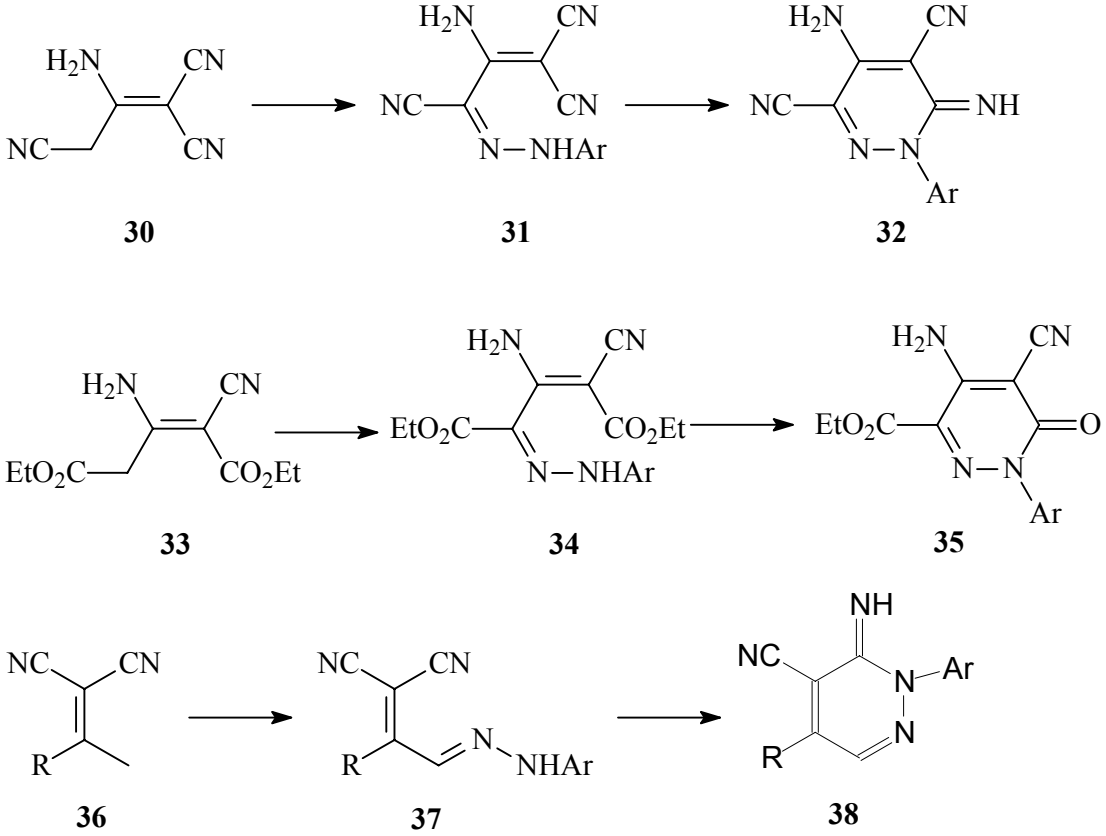
Scheme 5

The methylene functions in acetonitriles and benzylcyanide are not sufficiently reactive toward aromatic diazonium salts attempted coupling of cyanoacetic acid with aromatic diazonium salt affords only formazans **17.**[73,74] However acetonitrile derivatives **18-23** readily couple with aromatic diazonium salts to yield the corresponding arylhydrazones **24-29**[75-86] whose configuration have not yet been defined with certainty although structures have been assumed (Scheme 6).


NC—CH2—CO2H
ArN≡NCl
NC
N—NHAr
N=NAr
17
X
CN
18a: X = H
b: X = NO2
X = H
No reaction
X = NO2
24
19a: X = NH
b: X = S
25
20
26
21
27
22
28
23
29
R
X
Ar
HN

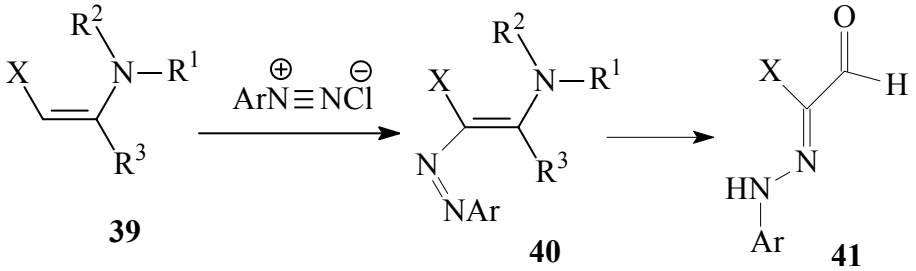
Scheme 6

The methylene group in **30, 33** and **36** also couples with aromatic diazonium salts to yield intermediate functionally substituted arylhydrazones **31, 34** and **37** that readily cyclize into pyridazines **32, 35** and **38** (cf. Scheme 7).[87]



Scheme 7

Enamines **39** couple with aromatic diazonium salts to yield 2-arylhydrazonoaldehyde **41** [88-99] and arylhydrazonoketones in excellent yield. An intermediate derivative **40** is believed to be formed in all cases and could sometimes be isolated (Scheme 8).

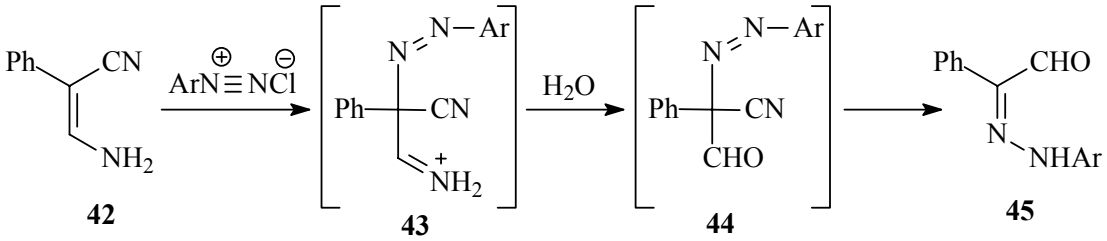


X = H ;COR^4, CO_2Et, CHO, CN

R^3 = H, Me; R^1, R^2 = H, alkyl

Scheme 8

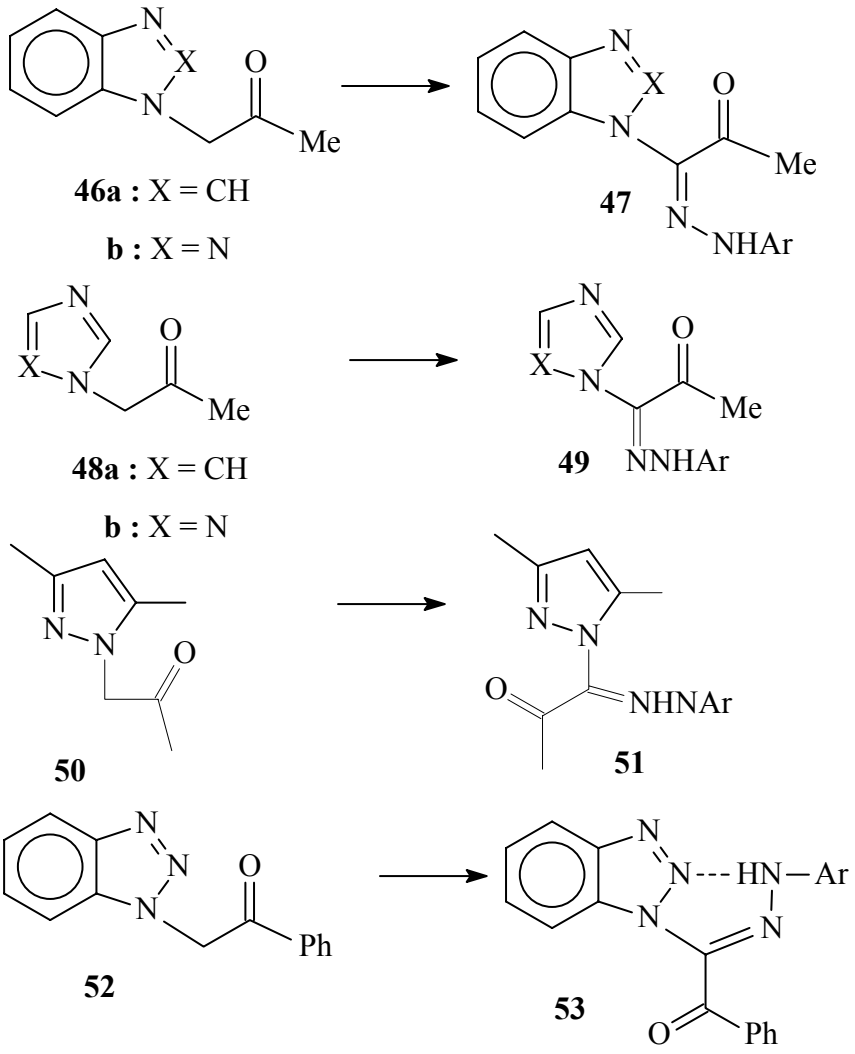
It has been recently observed that **42** couples with aromatic diazonium salt to yield arylglyoxal-2-arylhydrazones **45**. Formation of intermediate iminium ion **43** is believed to hydrolyze to **44** that undergo a Japp-Klingemann cleavage to **45** (cf. Scheme 9).[100]



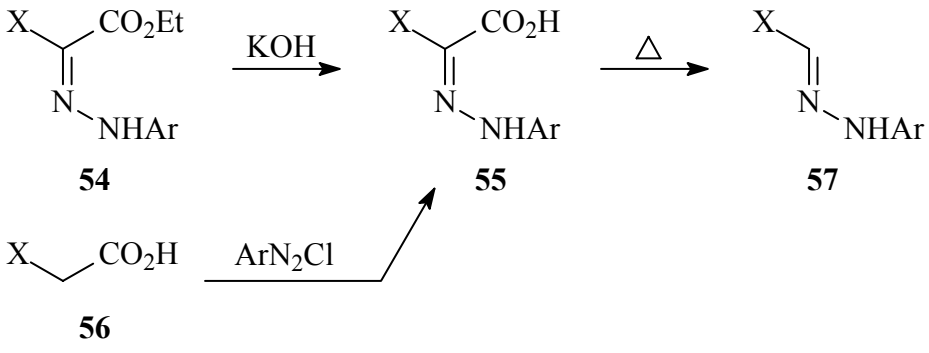
42 **43** **44** **45**

Scheme 9

Recent research at Kuwait and Cairo Universities showed that *N*-acetonylazoles **46a,b**, **48, 50** and **52** couple readily with aromatic diazonium salts to yield arylhydrazonals **47. 49, 51** and **53**[101-107] whose stereochemistry have not been defined. Phenacylbenzotriazole **52** has been coupled with aromatic diazonium salts to yield **53** that was suggested to exist in a (Z)-form. This form is stabilized by H-bonding with benzotriazole N-2 (cf. Scheme 10).[108]



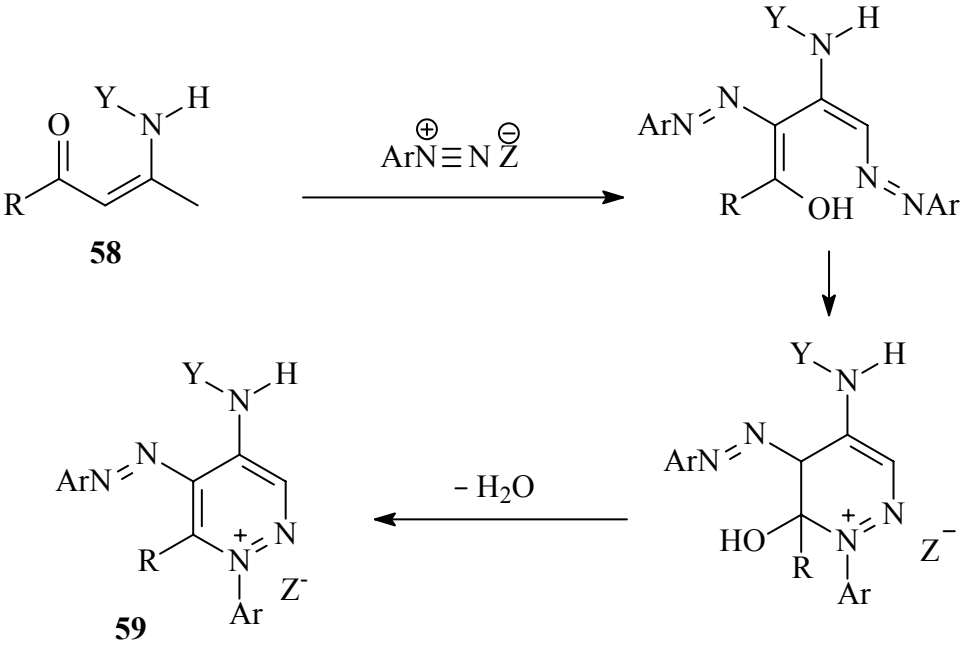
Scheme 10



Scheme 11

Functionally substituted arylhydrazones of type 1 where either X or Y = H are generally prepared from the corresponding esters **54** via conversion into the acid **55**[109-124] and subsequent decarboxylation to give **57**.[125-132] One step synthesis from the appropriate acids **56** has also been reported (c.f. Scheme 11).[133,134]

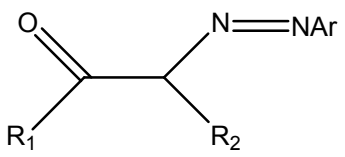
Interestingly coupling the enaminones **58** with aromatic diazonium fluoroborates have afforded **59**. The structure of this unexpected product is supported by X-ray crystallography. It is believed to be formed via intermediacy as shown in Scheme 12.[135,136]



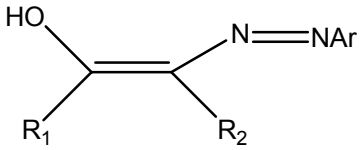
Scheme 12

3. Structure Investigation

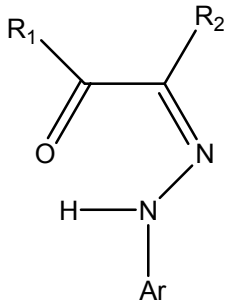
α-Oxohydrazones may exist in azo form **60a**, eneazo form **60b**, (*Z)*- and (*E)*-hydrazone forms **61a** and **61b**. From time to time different methods utilizing roles variable for chemists by time presented at a supporting existence of these compounds in hydrazone form (cf. Scheme 13).



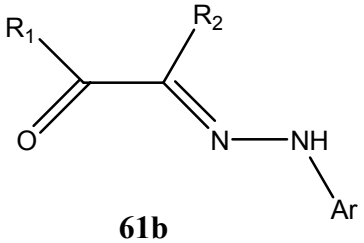
60a



60b



61a



61b

Scheme 13

Thus, it was assumed by Bamberger *et al.*[137] that (*Z)*-phenylglyoxal-2-nitrophenylhydrazones could be distinguished from the (*E)*- isomer by its relatively lower melting point, as in (*E*) recently H-bonding decrease tendency for association through intramolecular hydrogen bonding greater stability in certain solvents like benzene, deeper shade of colour and ease of crystallization.[137]

Some authors believed that phenylhydrazones having a strong internal hydrogen bonding has a lower carbonyl band frequency in IR.[138] This finding was utilized to differentiate between the (*Z*) and (*E)* forms of pyruvamide phenylhydrazone.[139] The (*E)* form showed the carbonyl band at higher frequency than that of the (*Z)* form. On the other hand, IR studies[140] of phenylglyoxalarylhydrazones indicate that the isomeric (*Z)* and (*E)* forms of these compounds can be easily distinguished by the position of the carbonyl as well as the NH stretching bands. Tanner[141] found that the carbonyl frequencies of both the (*Z)* and (*E)* forms of phenylglyoxal-2-nitrophenylhydrazone were almost the same (1641 and 1640 cm^{-1}, respectively) and that there was only a little difference in the NH stretching frequencies of these isomers (3128 and 3166, respectively).

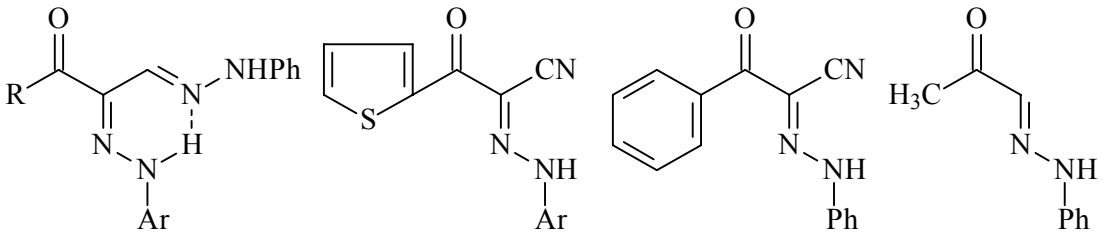
The NMR of the hydrazone NH of α-oxophenylhydrazones appears at δ 12-14 ppm. Studies of the isomeric forms in different solvents indicate that the equilibrium shifts in favor of (*E)* form in solvents that favor hydrogen bonding formation.

The structure of phenyhydrazones of four α-dicarbonyl compounds were determined from the IR and NMR spectra of the ^{14}N and ^{15}N isotopes. The compounds exist only in the phenyhydrazone tautomeric form and, except for the phenyhydrazones of phenylglyoxal in solution, primarily as the geometric isomer with the NHC_6H_5 group oriented away from the

carbonyl. The effect of solvent on the composition of the geometric isomerism equilibria was discussed.[142] El-Ashry *et al.*[143] concluded that these compounds exist mainly in chelated hydrogen bonded form.

In the light of recent x-ray crystallography by Elnagdi *et al.*[144-15-46] that arylhydrazono-3-oxoalkene nitriles exists in (*E)* form to make up for stereo electronic requirements previous conclusions about structure of arylhydrazo-ketones and ketoester should be rechecked (cf. structures **62-65**).

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 atom electron rich. In support of this view ^{1}H-NMR of phenylazomalononitrile showed NH signal at δ 13.0 ppm. Here hydrogen bonding is not possible.



62 **63** **64** **65**

Scheme 14

4. Chemical Reactivity

4.1. Introduction

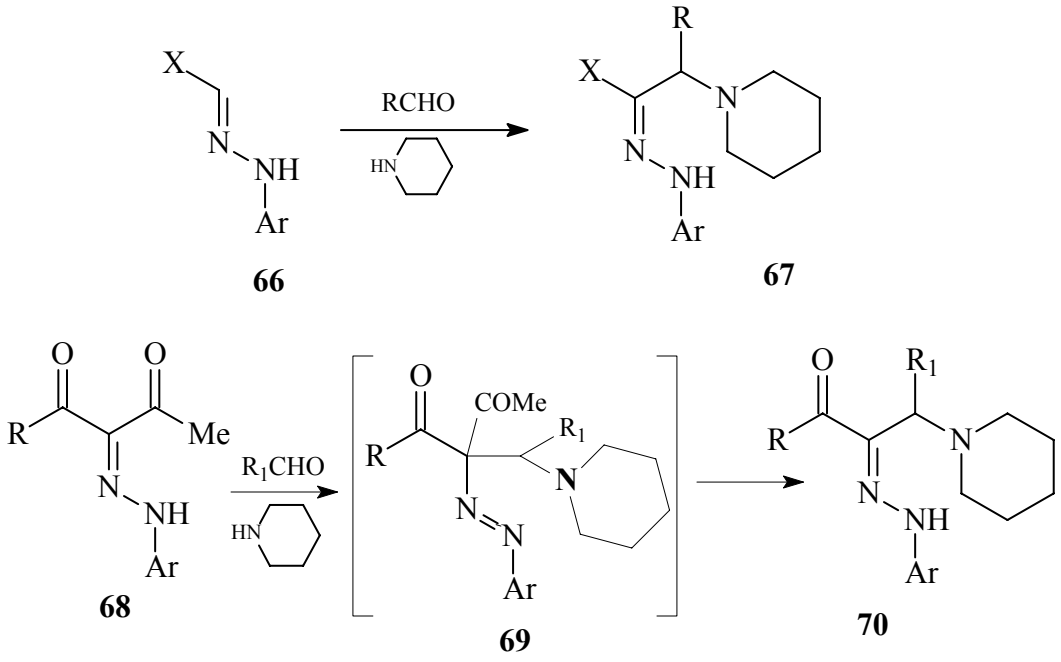
The most significant reactivity is the nucleophilicity of hydrazone carbon atom. This was noted since more than hundred years. Thus reactions like Mannich reaction, coupling reaction and halogenation have took place readily at such carbon. Recently Michael type addition was also described. Hydrazone nitrogen atom however remains the main site for attack by acylating and alkylating agents. It seemed that hard nucleophiles attack preferentially nitrogen atom, while soft ones attack preferentially at carbon atom.

The functional substituents retain their established reactivity pattern although generally become more electrophilic. Also multidentate reagents in several cases afford rings involving hydrazone moiety. In addition a variety of intramolecular cyclizations leading to cinnolines have been reported. In the following we will survey reported chemical reactivity pattern.

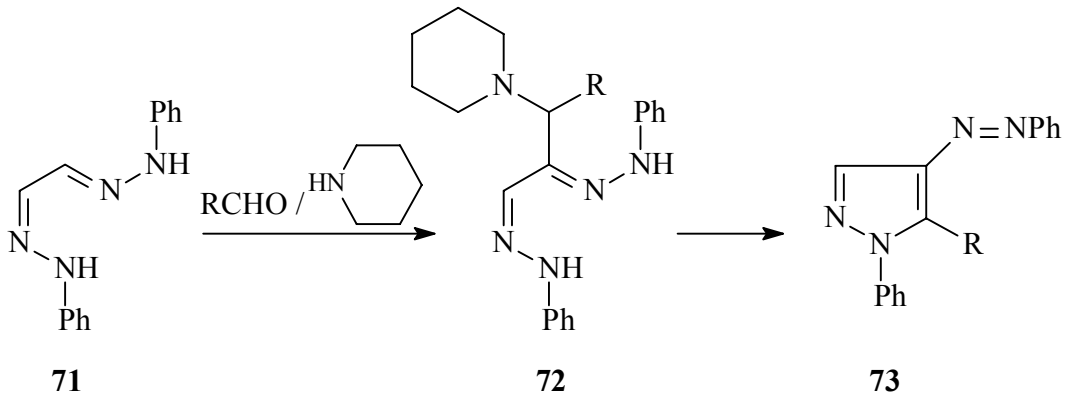
4.2. Reaction with electrophilic reagents

4.2.1. Reaction with carbon electrophiles

The reaction of α-ketohydrazones with Mannich reagents have been reported in the last century (c.f. formation of **67** from **66** is Scheme 15). Mustafa *et al.*[147] have shown that **68** undergo Mannich reaction at hydrazone carbon atom to yield intermediates **69** that readily undergo Japp-Klingemann cleavage yielding **70** in good yields. This reaction has recently been adopted to aromatic aldehydes.[147-151]



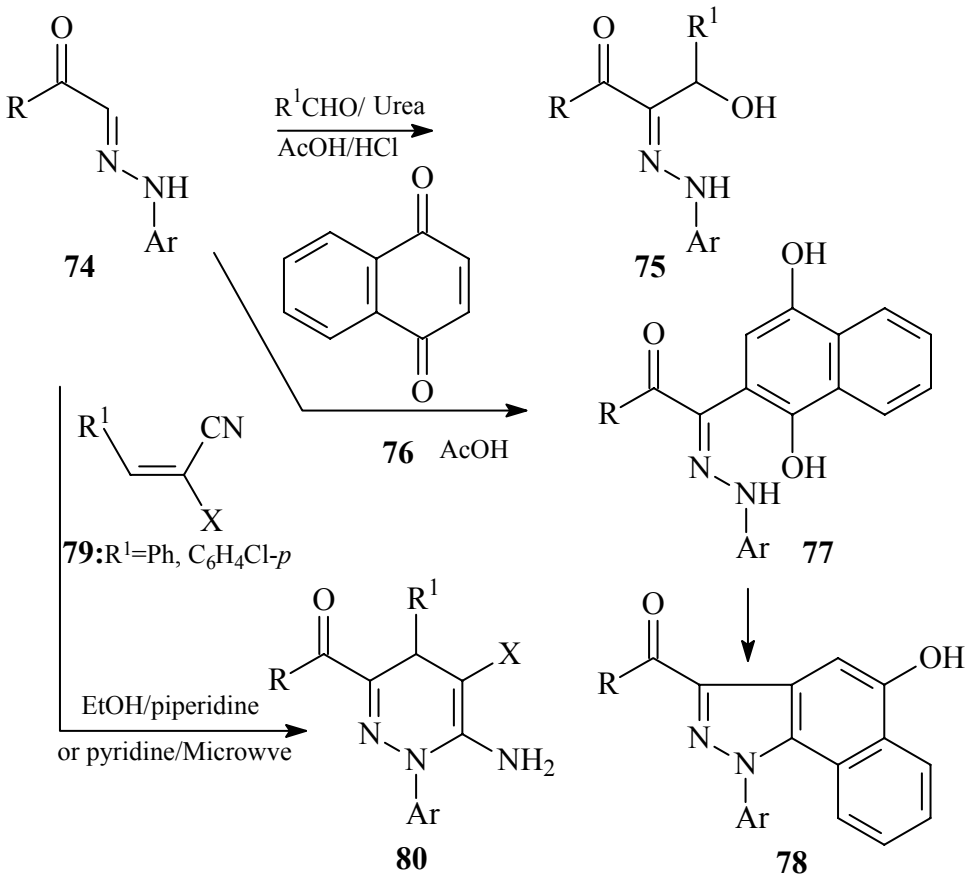
Scheme 15



Scheme 16

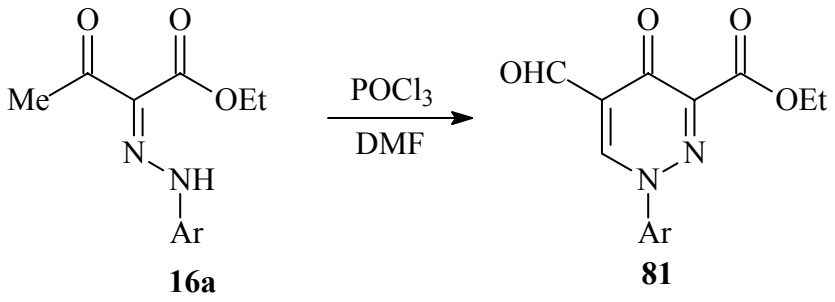
Glyoxaldiphenylhydrazone **71** also react with Mannich bases to yield either **72** or **73** depending on nature of utilized aldehyde (cf. Scheme 16).[152-154]

Aromatic aldehydes also react with **74** to yield **75**. In absence of urea the reaction does not proceed. Naphthoquinone **76** reacts with **74** to yield either **77** or **78** depending on applied reaction conditions. Cinnamonitriles **79** also reacted with **74** to yield dihydropyridazines **80** (cf. Scheme 17).[155]



Scheme 17

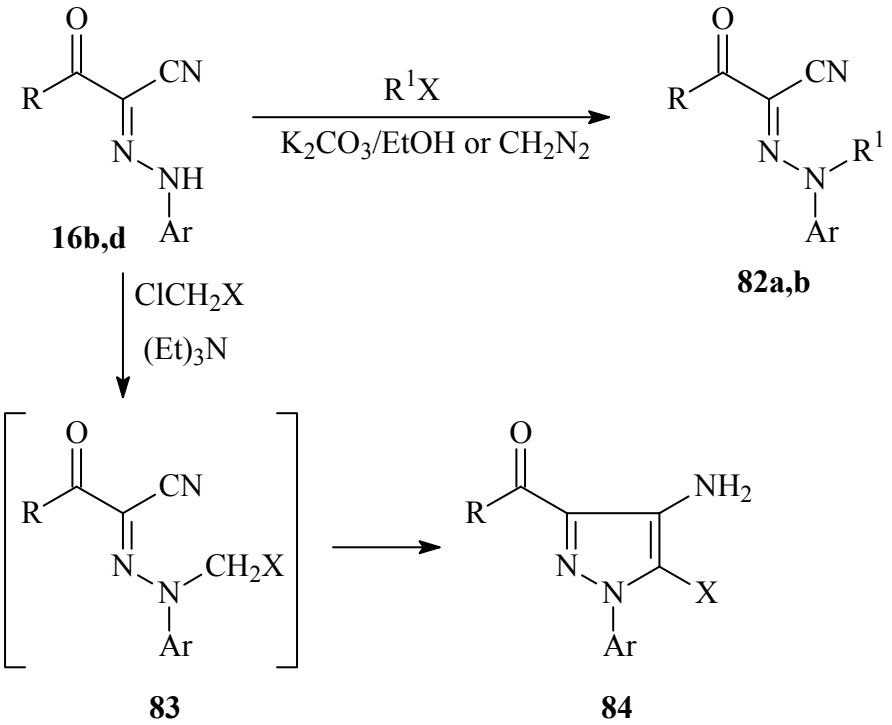
Treatment of ethyl 2-phenylhydrazono-3-oxobutanoate **16a** phenylazoethyl-acetoacetate **16a** with Vilsmeier reagent affords pyridazine carboxylic esters **81** (Scheme 18).[156]



16a **81**

Scheme 18

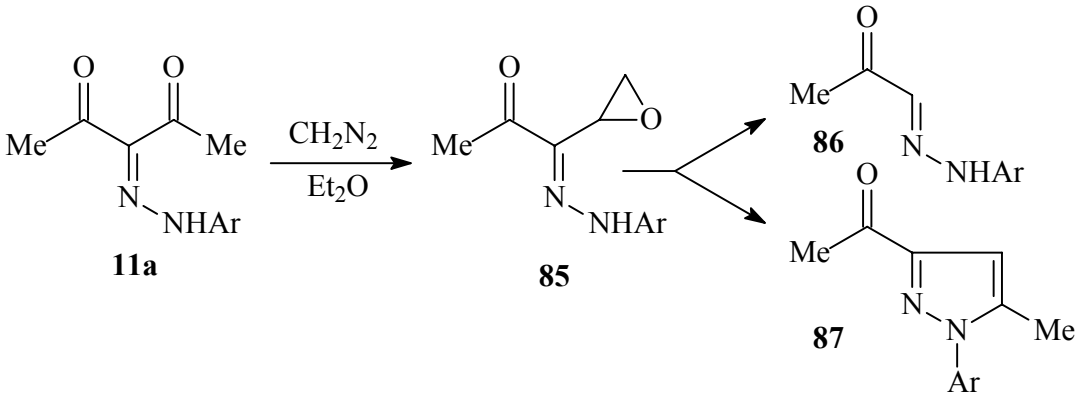
In contrast to reported reactivity at carbon in this reaction, treatment of **16b,d** with alkylhalides affords N-alkyl derivatives **82a,b**[157-159] The reaction of **16b,d** with chloroacetone, chloroacetonitrile or ethyl chloroacetate affords aminopyrazoles **84**, most likely, via intermediacy of non isolable acyclic **83.**[160]



16b,d **82a,b** **83** **84**

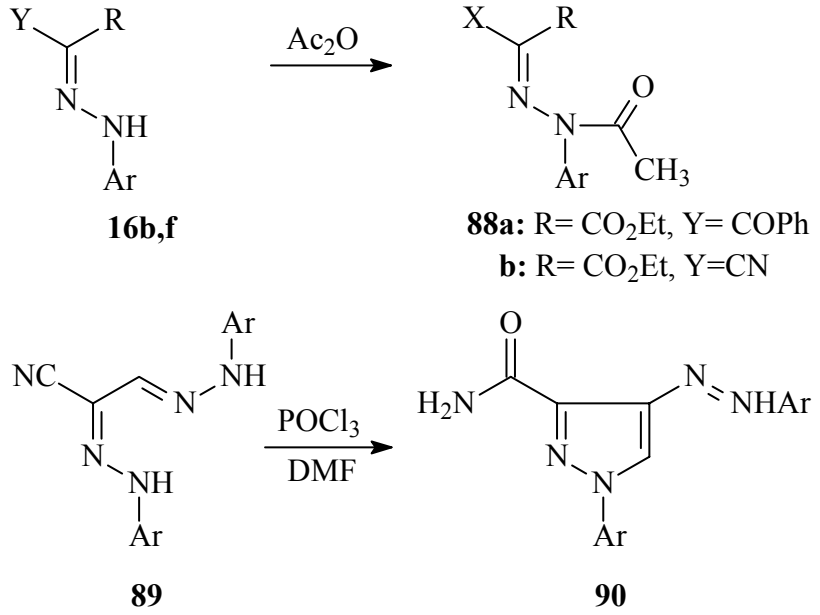
Scheme 19

The reaction of 3-(2-phenylhydrazono)pentane-2,4-dione **11a** with diazomethane afforded pyrazole **87** in addition to **85** and **86.**[161,162] Although reaction sequence looks logical, this result should be checked again and reaction product should be characterized spectroscopically.

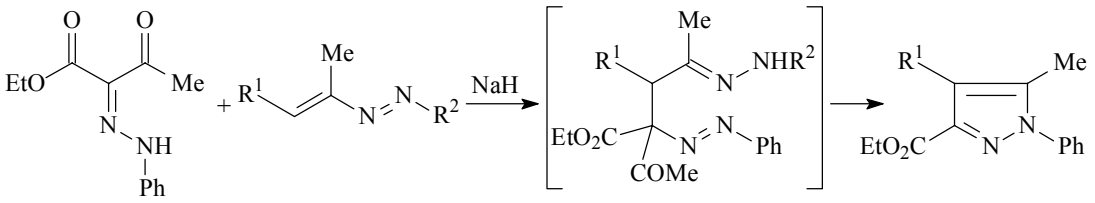


Scheme 20

Acetylation of **16b** and **16f** (R=CO_2Et, Y= COPh) give **88a,b** in good yield.[163,164] Recently Elnagdi et al[165] have reported both N and C-acetylation and benzoylation of glyoxal diphenylhydrazones. Successful Vilsmeier formylation of **89** followed by cyclization and hydrolysis to yield pyrazole **90** has been also recently reported.[166]



Scheme 21

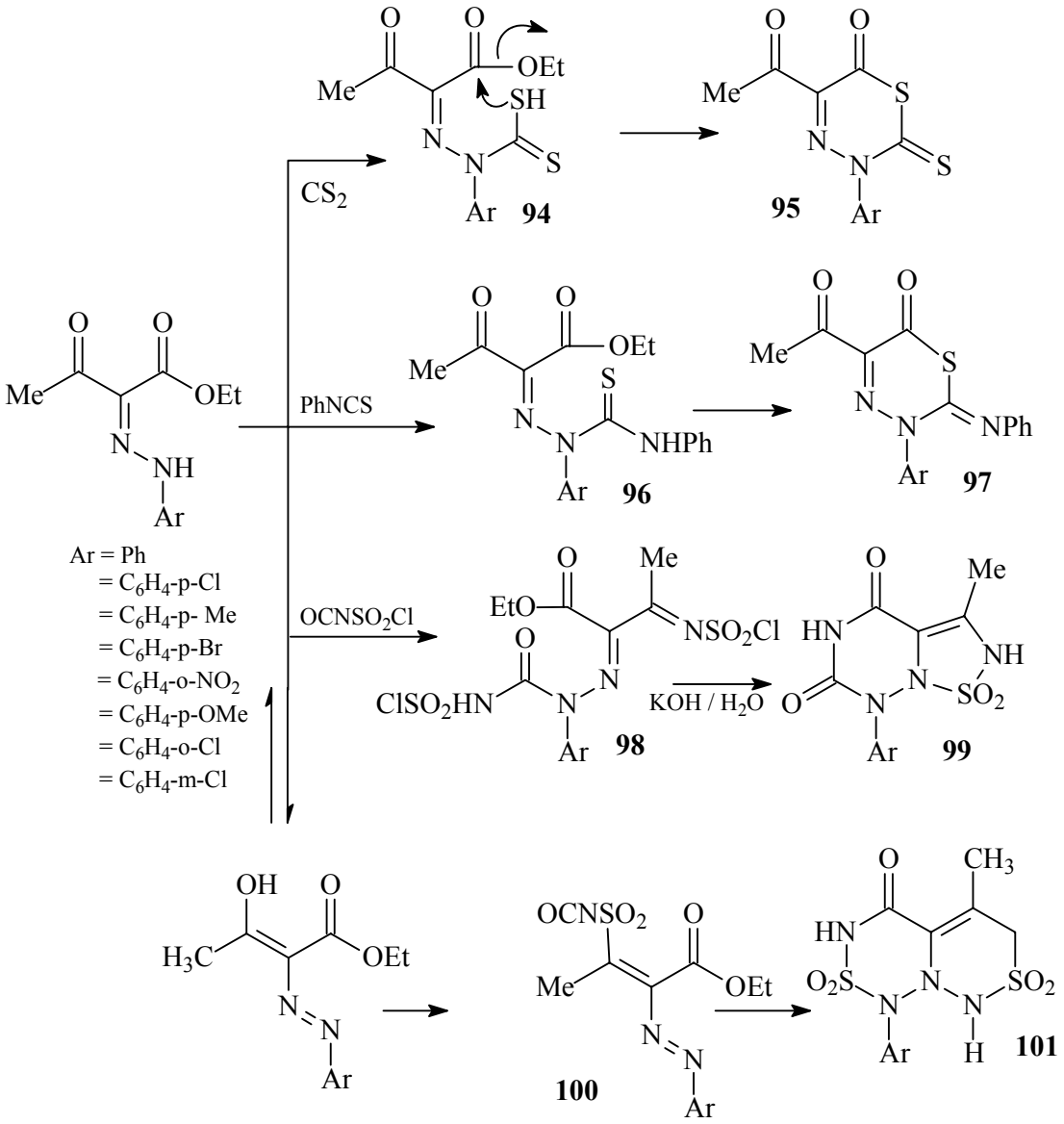


16a **91** **92** **93**

Scheme 22

The azadiene **91** reacts with **16a** to yield the pyrazole **93**. Initial formation of adduct **92** is postulated.[167]

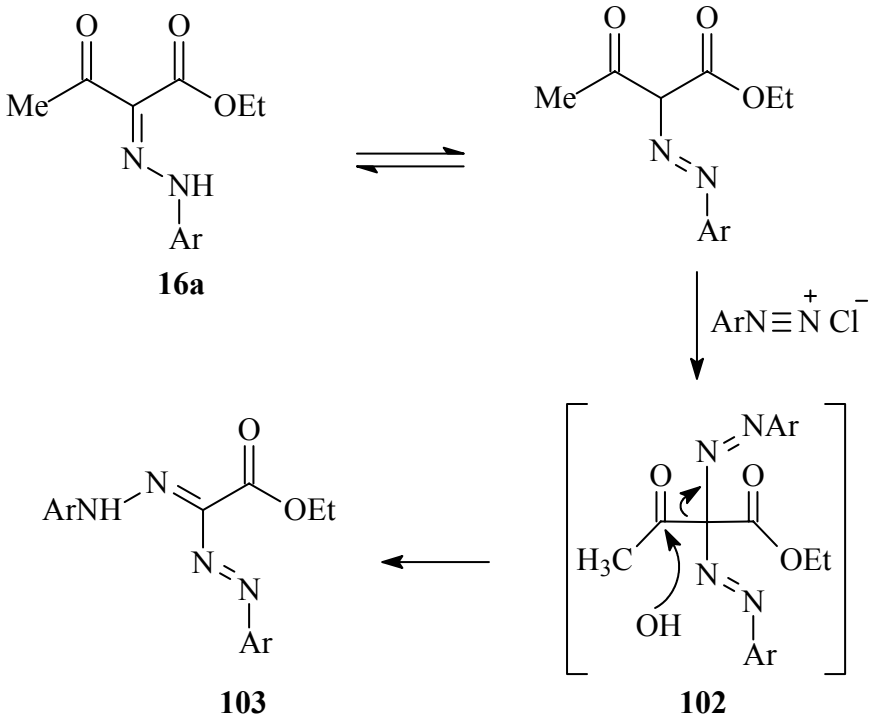
The hydrazone nitrogen atom is the preferred site of attack by electrophilic *sp* carbon atoms. Thus carbon disulphide reacts with **16** to yield **95** via intermediate **94**. similarly phenylisothiocyanate affords **97**, most likely via intermediate **96**. The reaction of **16** with chlorosulfonylisothiocyanate affords at 0-5 °C the chlorosulphonyl derivative **98** that is readily cyclized into **99** by aqueous KOH in presence of thiophenol. At 105-110 °C however enol form of **16** affords **101** via intermediacy of **100.**[168,169] It should be mentioned however that in absence of conversing spectral evidence supporting these structures reported conclusions seems highly unlikely. For example **97** can also cyclized to 1,2,4-triazine formation of N-N bonds or N-S bonds as well as highly strained non aromatic heterocycles seems in light of modern knowledge least likely**.**



Scheme 23

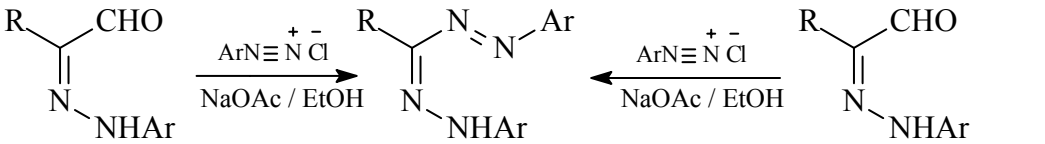
4.2.2. Reaction with nitrogen electrophiles

Coupling occurs at hydrazone carbon atom and formed bisazo in case of hydrazones of type **1** coupled normally undergo a Japp-Klingemann cleavage of a functional group. Thus, **16a** couple with aromatic diazonium salts to yield intermediate **102** that is directly converted into the isolable formazane **103.**[170]



Scheme 24

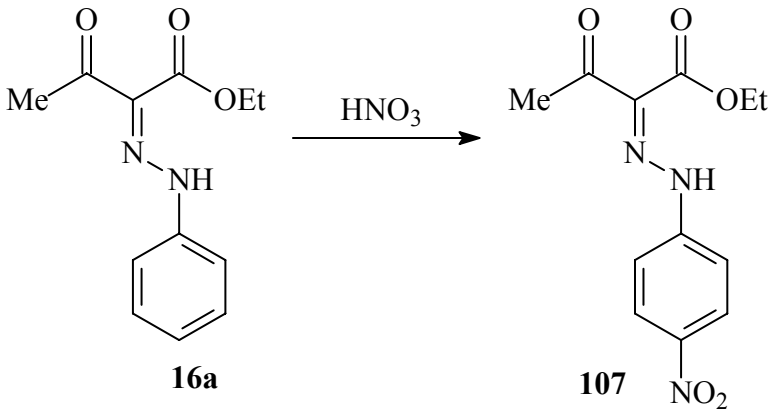
Formation of formazan **106** has been also observed upon coupling arylhydrazonoaldehyde **104a,b** and/or **105** with aromatic diazonium salts (c.f. Scheme 25).[171,172]



104 R = COC_6H_4Cl-*p* **106** **105** R= CN

Scheme 25

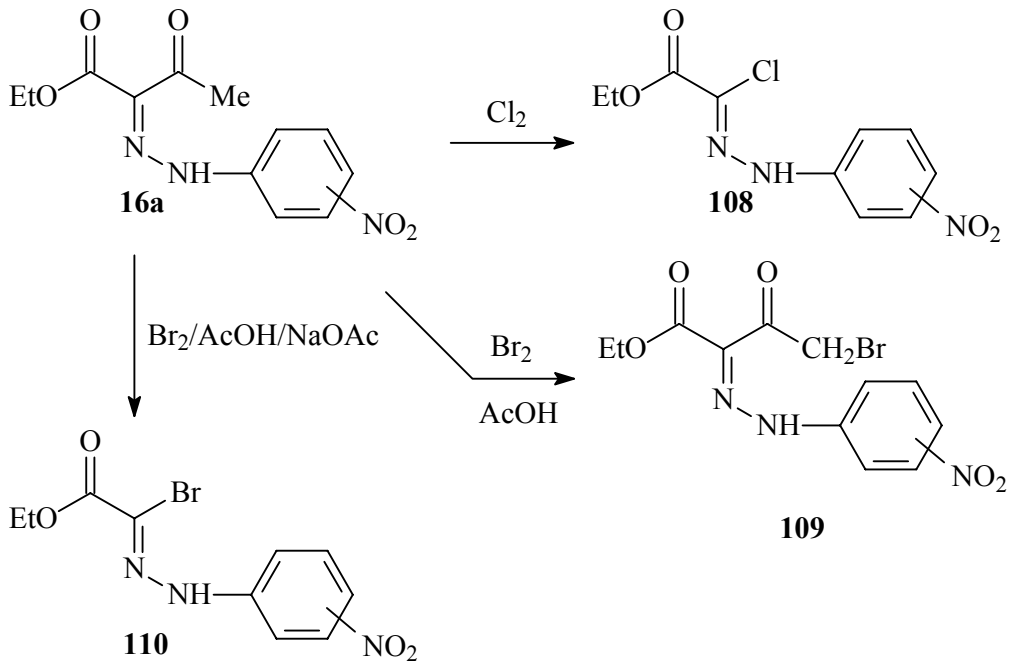
Ethyl 2-phenylhydrazono-3-oxobutanoate **16a** is readily nitrated at phenyl moiety on treatment with nitric acid to give **107.**[24]



Scheme 26

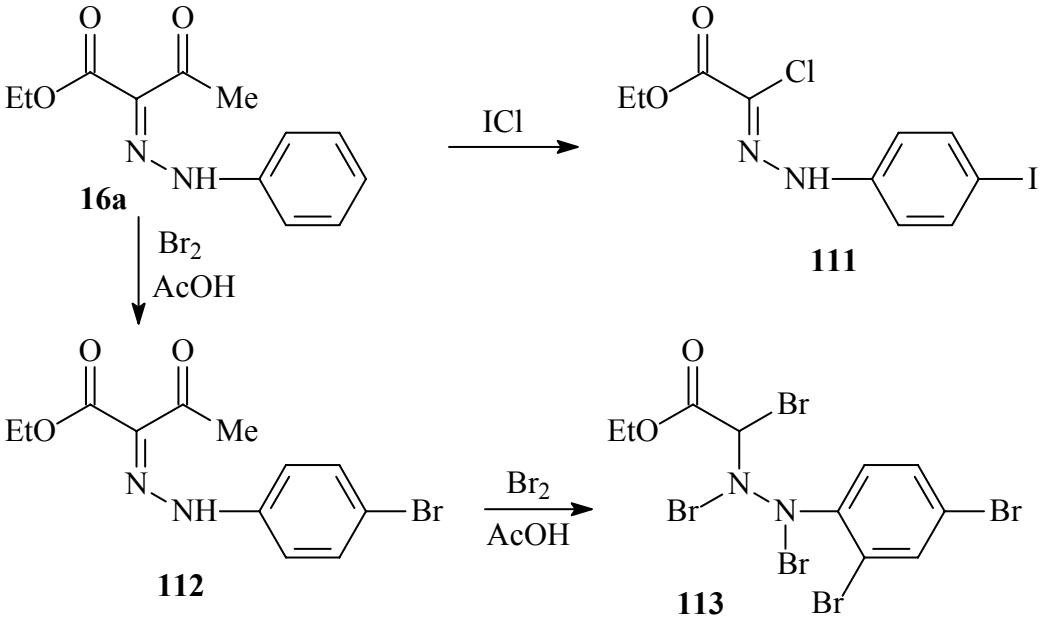
4.2.3. Reactions with halogen electrophiles

Halogenation occurs either at hydrazone carbon or at aryl or alkyl moieties depending on the nature of substituents on hydrazone moiety. Normally in acetic acid and in presence of sodium acetate halogenation occurs at hydrazone carbon and is followed by Japp-Klingemann cleavage of one of the functional groups attached to hydrazone carbon. If the hydrazone aryl moiety carry a strong electron attracting substituent (e.g. nitro function) initial halogenation occur at alkyl moieties in the molecule when they do exist. For example chlorination of **16a** (Ar = $C_6H_4NO_2$) with chlorine gas gives the hydrazonyl halides **108**.[173-175] Bromine in acetic acid affords mono bromination products **109**. If bromination is conducted in acetic acid in the presence of sodium acetate bromination at hydrazone carbon followed by Japp-Klingmann cleavage yielding **110** occurs. We believe that under such basic conditions the reacting species is a molecule of **16** that is capable of delocalizing negative charge on hydrazone carbon making it thus sufficiently nucleophilic.[176-180]



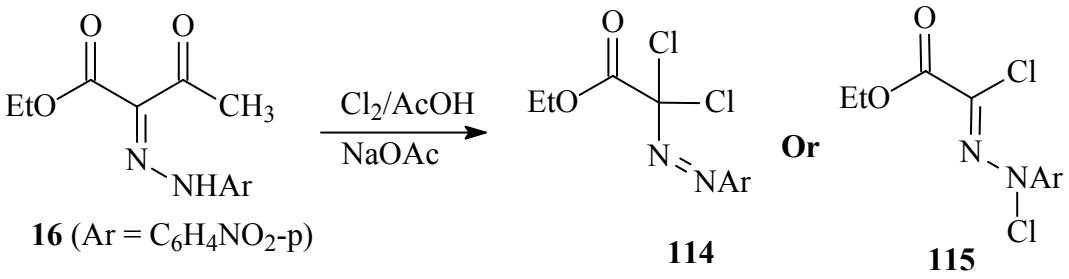
Scheme 27

It has been reported that if the arylhydrazone moiety is not substituted it can also participate in these reactions. For example chlorination of **16a** with iodine chloride gives product of attack at both hydrazone carbon and phenyl moiety yielding **111.**[181] Bromination of **16a** gives **112**. Utility of excess of bromine is believed to yield **113.**[182] Again spectroscopic evidence or X-ray crystallography is needed to support or revise these structures.



Scheme 28

Deviations from the general pattern have been reported. It seems that as a result of the fact that good part of these investigations has been made before development of appropriate spectroscopic methods for structural elucidation led in several cases in concluding structures with no solid evidence. For example chlorination of **16** (Ar= $C_6H_4NO_2$-p) has been claimed to yield **114**.[183] In other report chlorination in acetic acid in presence of sodium acetate gave **115**. We believe that concluded structure need to be reinvestigated.[173]



16 (Ar = $C_6H_4NO_2$-p) **114** **115**

Scheme 29

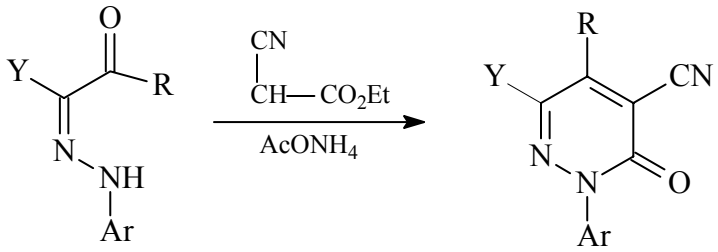
4.3. Reaction with nucleophilic reagents

4.3.1. Introduction

Plenty of condensations occur at carbonyl group in **1** and reactions of this type when both X and Y are carbofuncionallties lead to formation of arylazoheterocycles that are extensively utilized in dye industry. Condensation with bidentate reagents with electrophilic and nucleophilic moieties normally leads to pyridazine formation.

4.3.2. Reaction with carbon nucleophiles

Carbofuncion in ethyl 2-phenylhydrazono-3-oxobutanoate **16a** condenses readily with ethyl cyanoacetoacetate to yield pyridazinones. This reaction type has been extensively utilized for synthesis of various functionally substituted pyridazines.[184-191] Thus **16a,f,g** afforded **116a-e** while **16h,i** gave the dicyanopyridazineones. Condensation of **16a** with diethyl malonate also afforded diethyl pyridazine dicarboxylates. The reaction has been also conducted under microwave irradiation and afforded highly pure pyridazinone in much shorter time. [184-191]

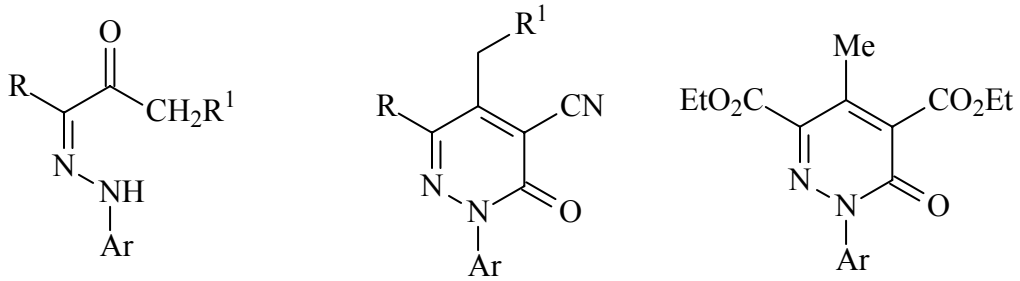


16a: R=H, Y= CO_2Et
b: R=Me, Y= CO_2Et
c: R=H, Y=CN
d: R=Me, Y= CN
e: R=Ph, Y=CN

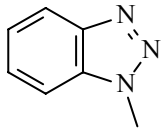
116 a-e

Scheme 30

Benzoylacetonitrile, cyclohexanone, cyanoacetamide and malononitrile were also condensed with arylazo derivatives to yield pyridazinones.[192] The benzotriazolyl derivative **117** and the hydrazonopyruvate also condense with ethyl cyanoacetate to yield **118** and **119,** respectively.[186]



117a: R =

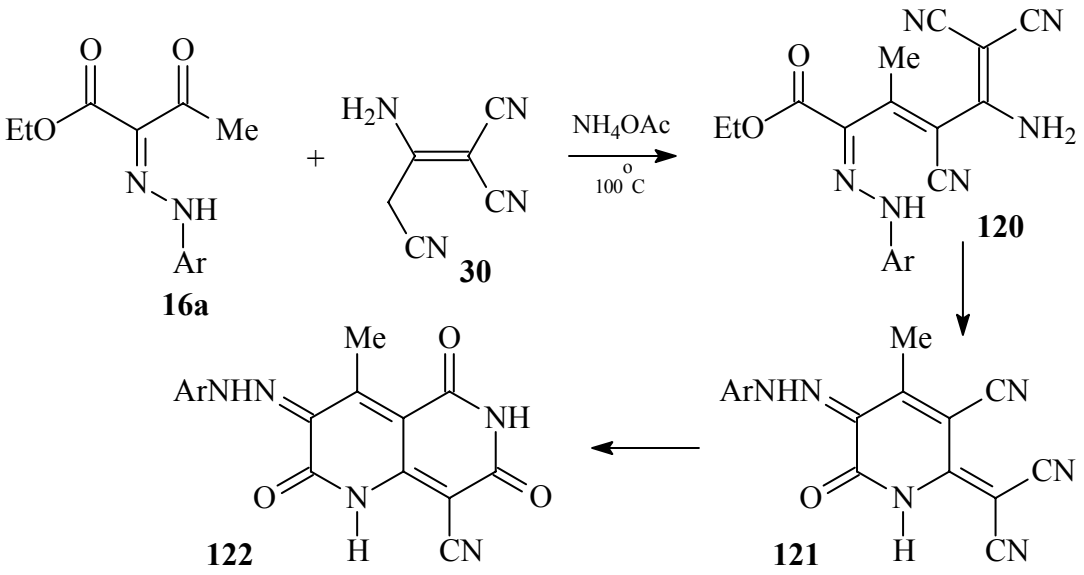


b: R = H, Me

118 **119**

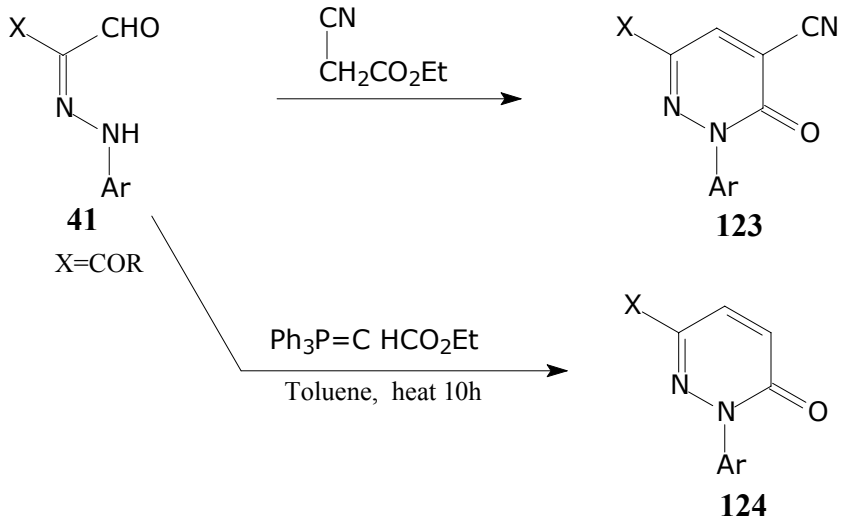
Scheme 31

Condensation of **16** with 2-aminoprop-1-ene-1,1,3-tricarbonitrile **30** gives **122** via **120** and **121**.[193,194] Although this work has been published recently, the luck of convincing spectral evidence to support these conclusions seems quite strange as several alternate structures looks also possible**.**



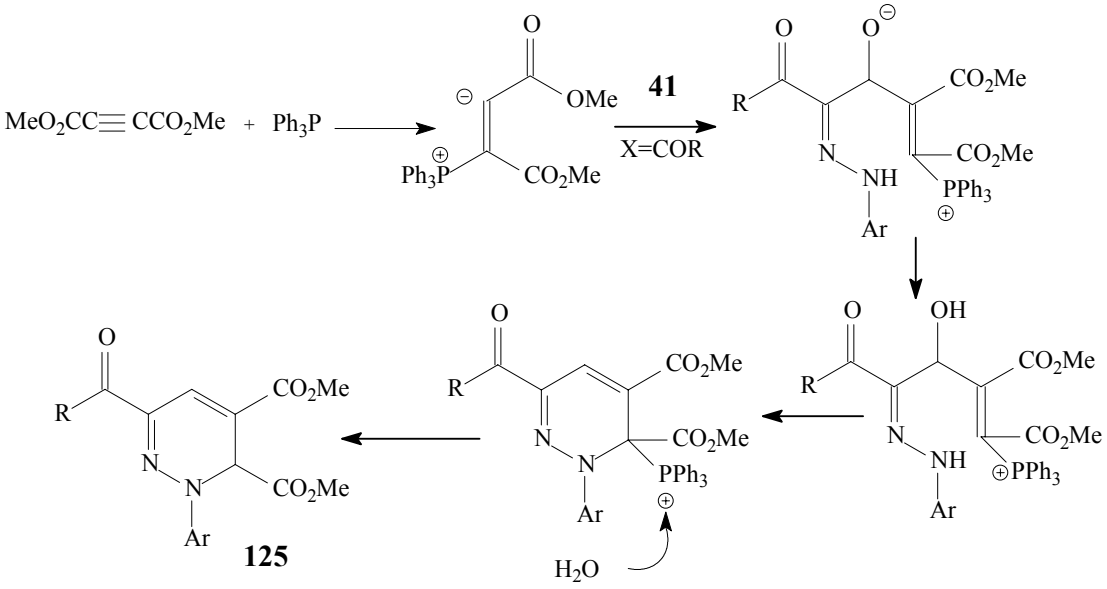
Scheme 32

The arylhydrazonals **41** also reacted with ethyl cyanoacetate yielding pyridazinones **123**. Wittigs reagents condense also with **41** to yield the corresponding pyridazinones **124** in good to excellent yields.[195,196]



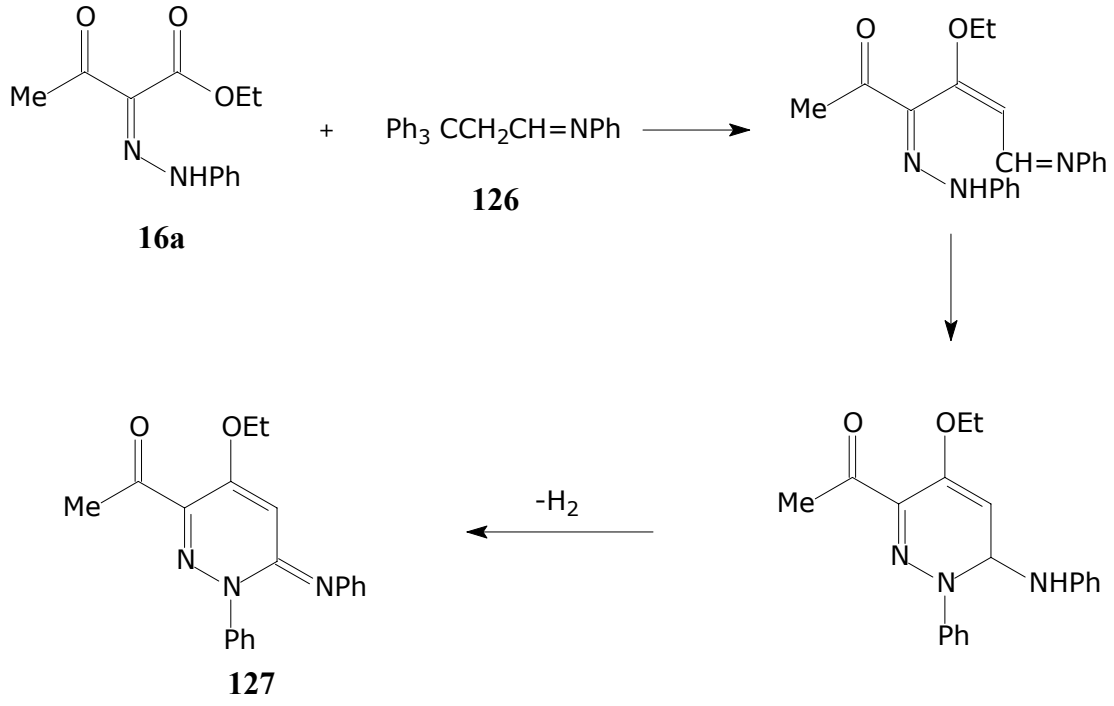
Scheme 33

A carbon Mitsunobu reaction of **41**; X = CHAr (or better a Baylis-Hillman like reaction) has been reported. Thus reacting **41**; X = COAr with dimethyl acetylene dicarboxylate and triphenylphosphine in methylene chloride gives the pyridazinedicarboxylates **125**. It is believed that this reaction proceeds via sequence shown in Scheme 35.[197,198]



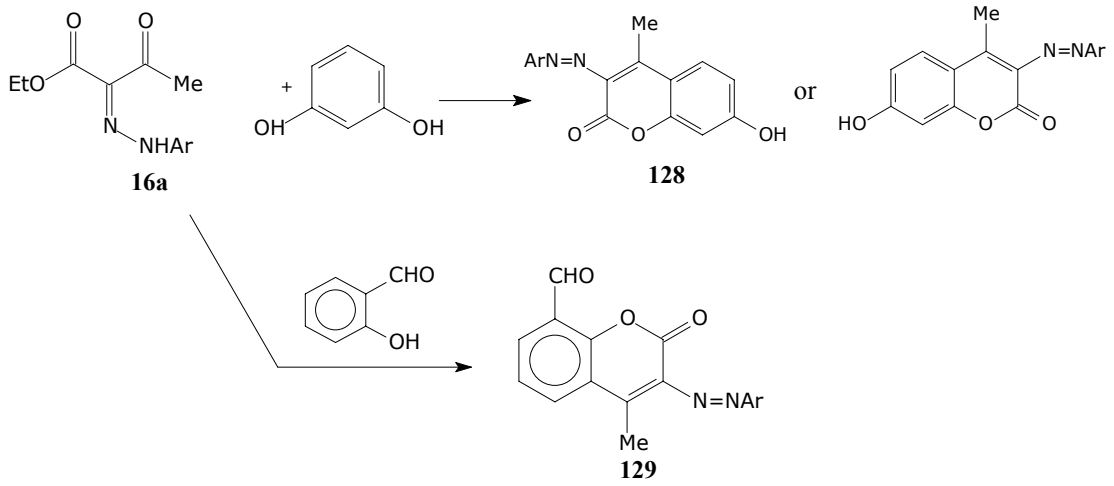
Scheme 34

The reaction of **16a** with **126** gives **127.**[199]



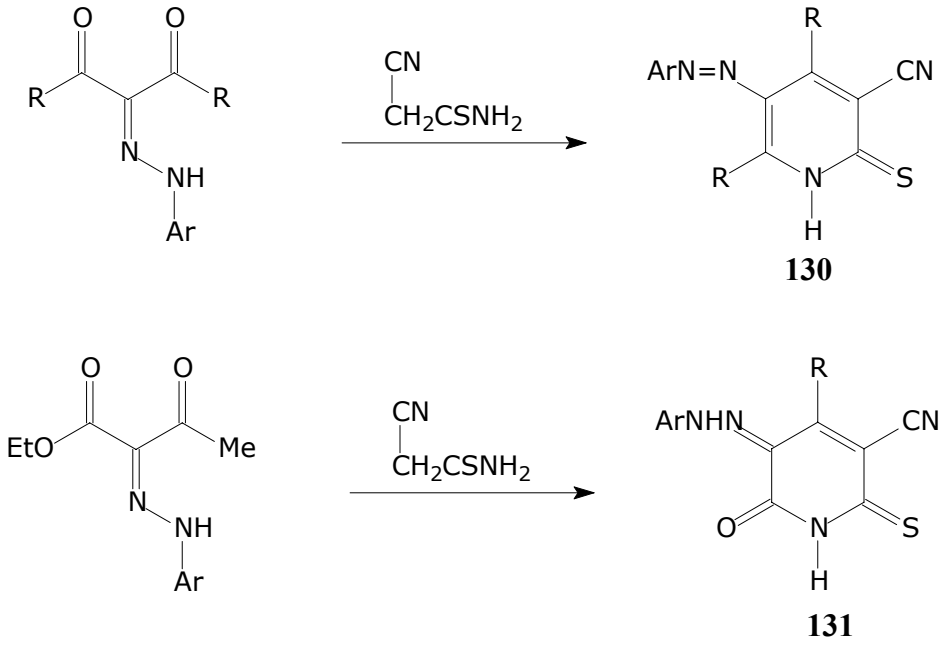
Scheme 35

Phenols condense with **16** to yield chromene derivatives. For example condensation of **16a** with resorcinol affords **128**, salicylaldehyde gives **129.**[35,37]



Scheme 36

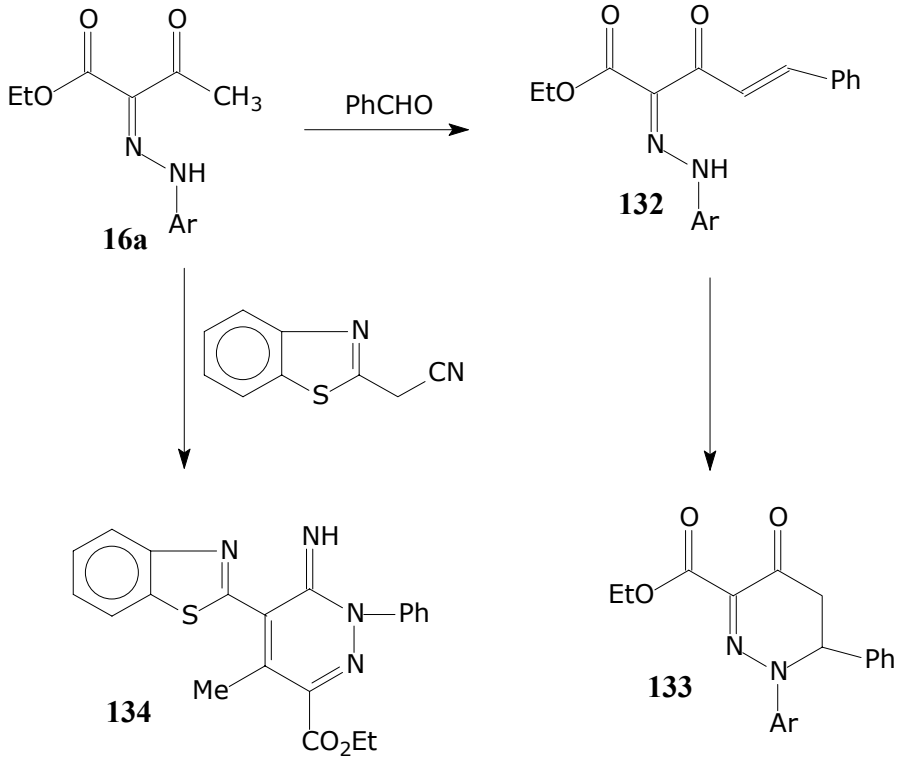
Cyanothioacetamide condensed with **16a,b** to yield **130** and **131,** respectively.[16]



Scheme 37

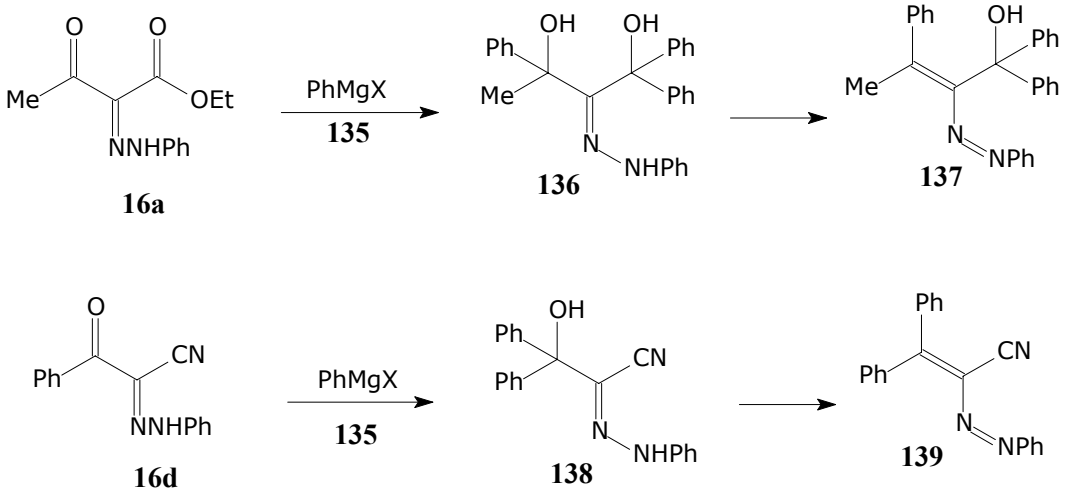
Benzaldehyde condenses with **16a** to yield pyridazinones **133**. Intermediate **132** could be isolated. Compound **133** can also exist in enol form or may also readily autooxidize into

aromatic pyridazinones. It seems that of value to reconfirm the suggested structure, condensation of benzothiazolylacetonitrile with **16** gives **134**.[186,200,201]



Scheme 38

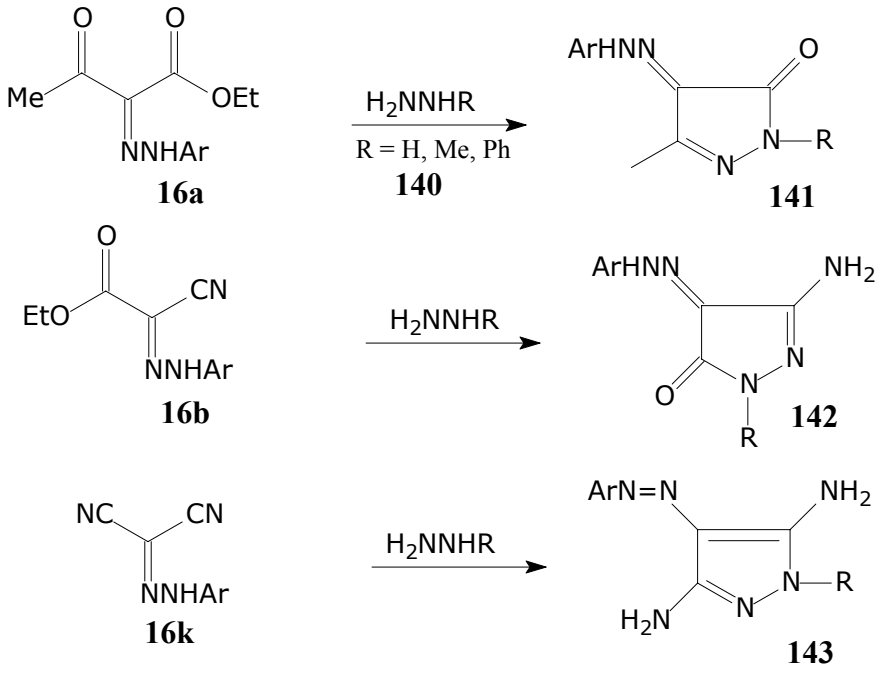
The reaction of Grignard reagent **135** with **16a,d** gives **136** and **138** which were readily dehydrated by reflux in acetic acid to yield **137** and **139**, respectively.[202]



Scheme 39

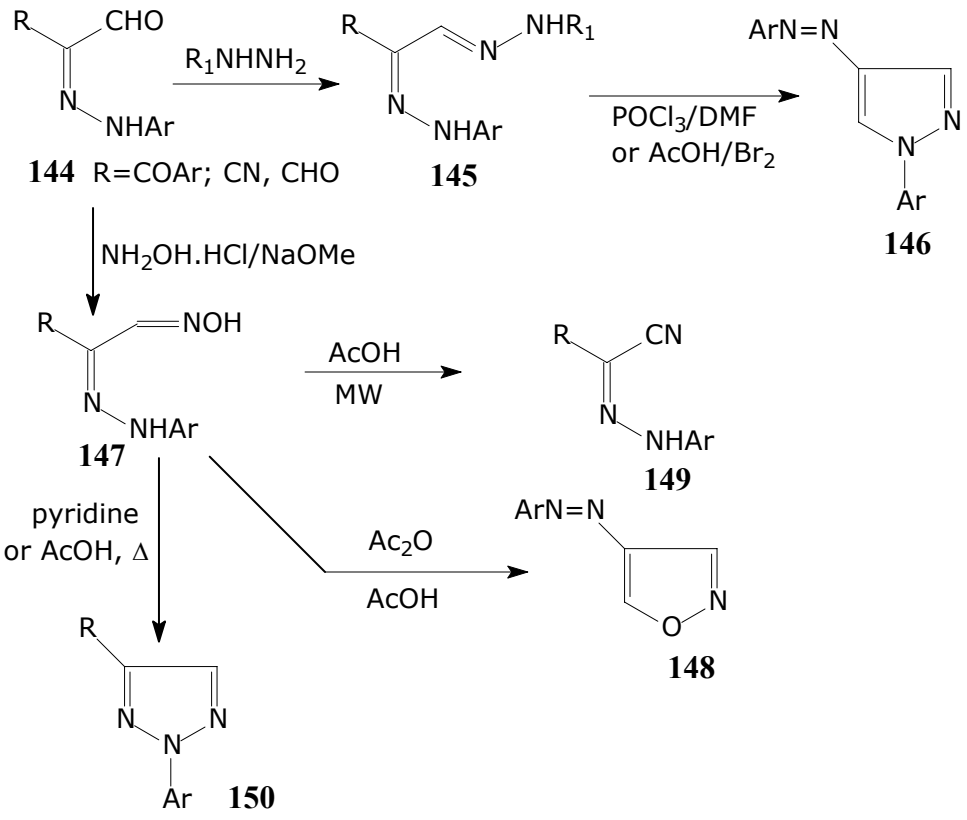
4.3.3. Reactions with nitrogen nucleophiles

These reactions have been extensively investigated in the literature because of potential utility of formed arylazo heteroaromatics in dye industry. Quite a number of arylazopyrazolones and aminoarylazopyrazoles is commercialized. It is well established that **16a,b,k** react with hydrazine derivatives **140** to yield pyrazolone **141** or arylazoaminopyrazoles **142** and **143.**[203-207]



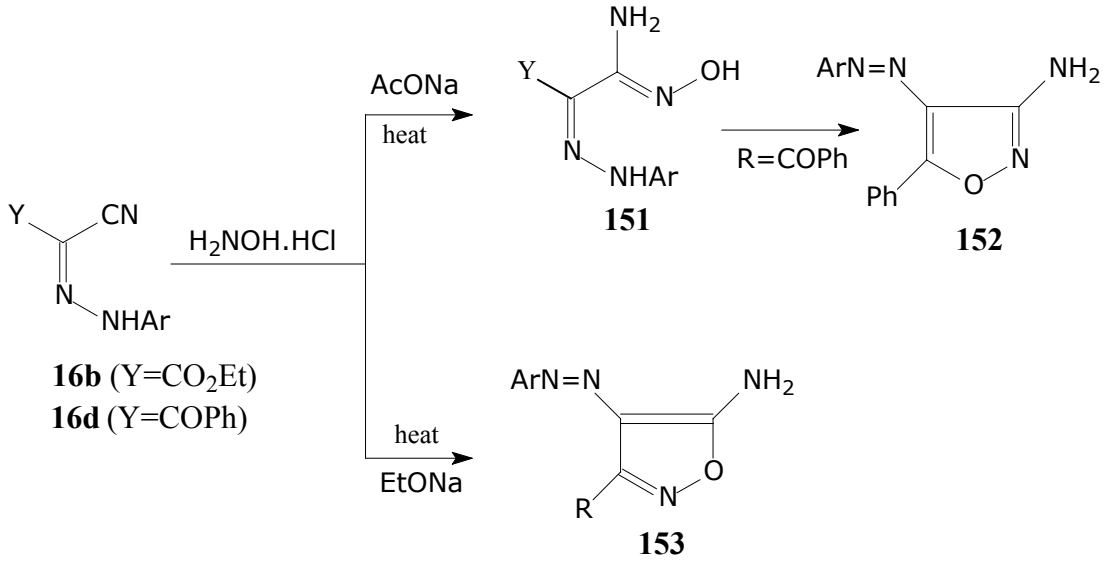
Scheme 40

Recently, however, Elnagdi *et al.*[208] have reported that reaction of **144** with hydrazines affords the stable hydrazones **145**. These could be cyclized only under drastic conditions into pyrazoles **146**[209-211]. It can thus be suggested that this is beyond the stability of these hydrazones. Hydroxylamine hydrochloride reacts with **144** in basic media to yield isoxazolones **148.**[212,213] However, again only oximes **147** were produced from reaction of **144** with hydroxylamine. The latter either cyclised into 1,2,3-triazoles **150**[214, 215] or were converted into nitriles **149** [216] by action of acetic acid. Only upon reflux in Ac_2O isoxazoles **148** were produced.



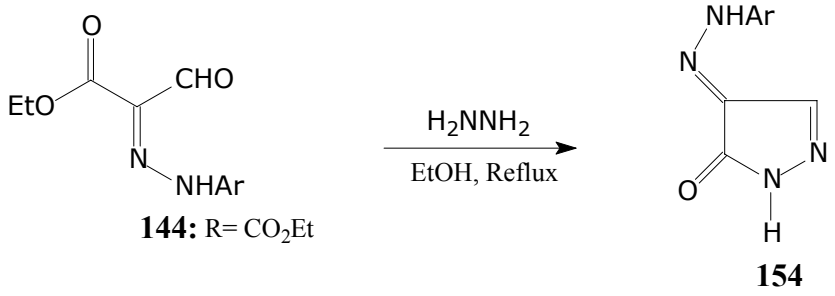
Scheme 41

The reaction of hydroxylamine hydrochloride with **16b,d** derivatives give amidoximes **151** that are converted into isoxazoles **152** upon reflux in ethanolic sodium ethoxide or treated with concentrated sulfuric acid. On the other hand when the reaction is conducted in ethanolic sodium ethoxide, isomeric 5-aminoisoxazoles **153** were produced. The dependence of the products on the applied reaction conditions is attributed to extra activation of cyano function in protic media.[217]



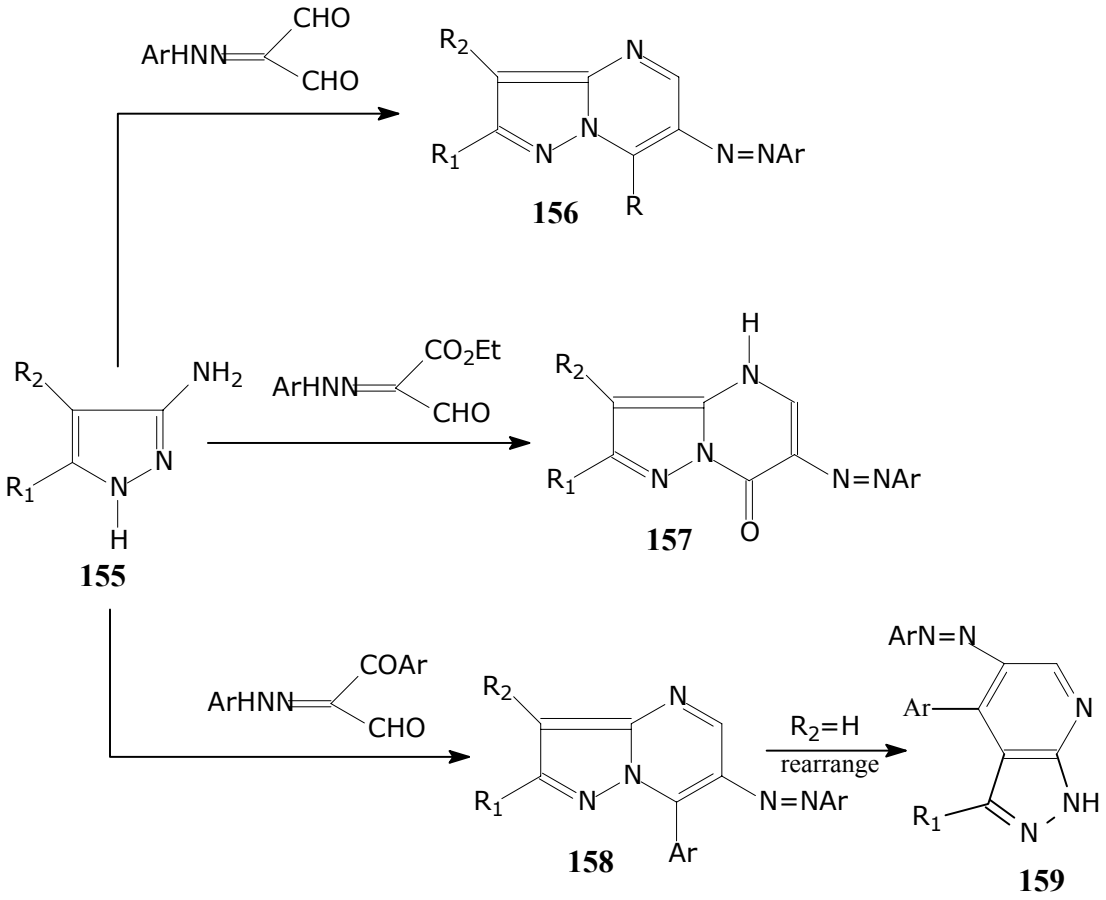
Scheme 42

The ester **144** afforded arylazopyrazoles **154** upon treatment with hydrazine hydrate in refluxing ethanol.[218,219]



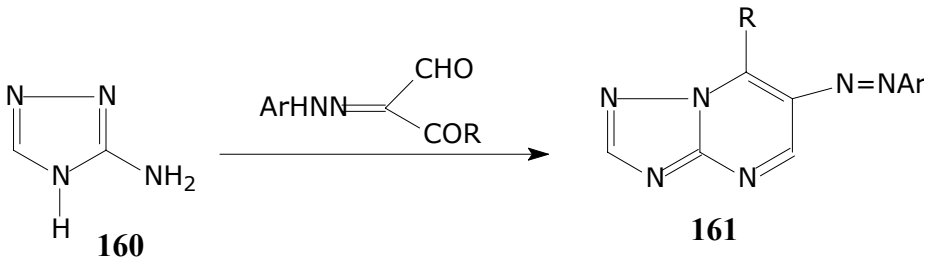
Scheme 43

Aminopyrazoles **155** condense with arylhydrazonals to yield pyrazoles[1,2-*a*] pyrimidines **156-158** that rearranged in some cases when C-4 in pyrazole is unsubstituted into pyrazoles[3,4-b]pyridines **159**.[16,220]



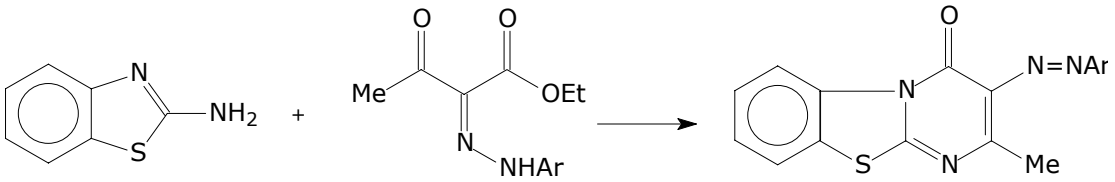
Scheme 44

In a similar way 1*H*-1,2,4-triazole-5-amine **160** reacted with arylhydrazonal to yield triazolo[1,5-*a*]pyrimidines **161**. The structure of these derivatives was established by x-ray diffraction analysis.[198,221,222]



Scheme 45

2-Aminobenzothiazole reacts with **16a** to yield **162.**[223]

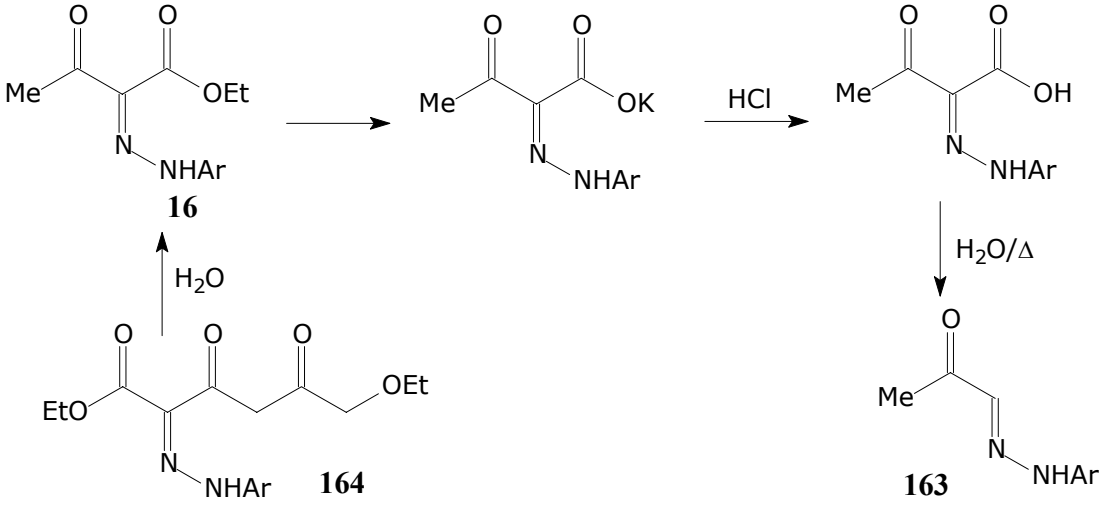


162

Scheme 46

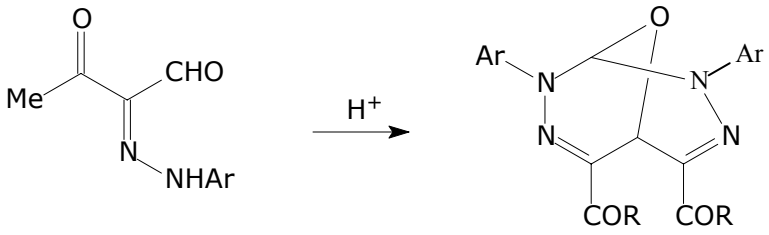
4.3.4. Reaction with oxygen nucleophiles

Hydrolysis of ester function in **16** and subsequent decarboxylation of the formed acid that readily decarboxylate into pyrovaldehyde-1-phenylhydrazone **163** by action of alcoholic or aquous sodium hydroxide is well established route to **163**. The diester **164** is readily converted upon treatment with water into **16.**[224,225] Again this old reaction should be rechecked as possible cyclization into pyridazin-4-one can not be overlooked.



Scheme 47

3-Oxo-2-arylhydrazonals **144** (R= COMe) are reported to dimerise readily upon reflux in acid media. The structure of the dimer **165** was confirmed by X-ray crystal structure determination.[170]

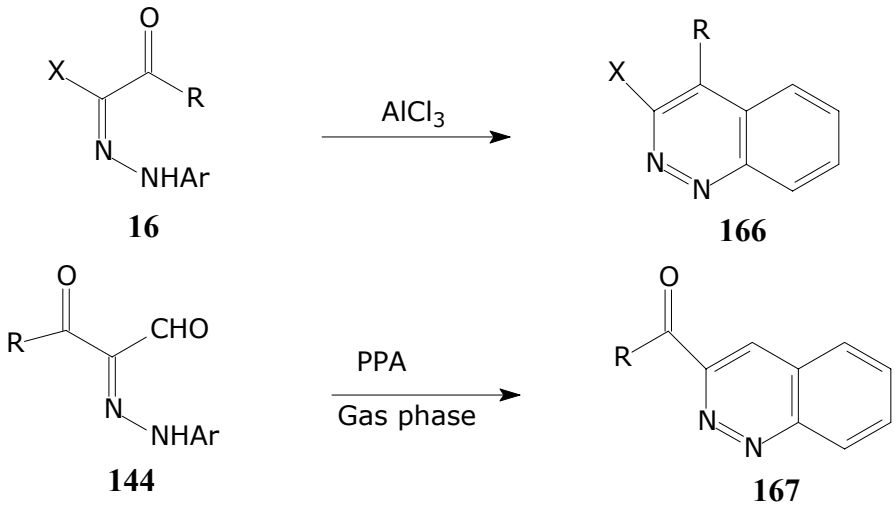


144 (R=COMe) **165**

Scheme 48

5. Intramolecular Processes

2-Oxoarylhydrazones **16** are readily cyclised in presence of Lewis acids into **166**. Similarly **144** are cyclised either by the action of polyphosphoric acid or upon pyrolysis in the gas phase into **167.**[226,227]

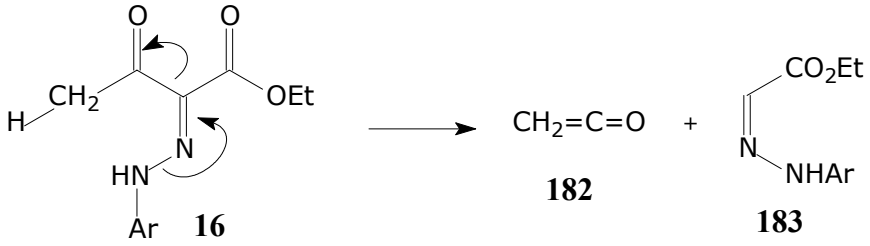


16 **166**

144 **167**

Scheme 49

Gas-phase pyrolysis of **16** gives **168** and **169** via a six-membered transition state.[17,228]

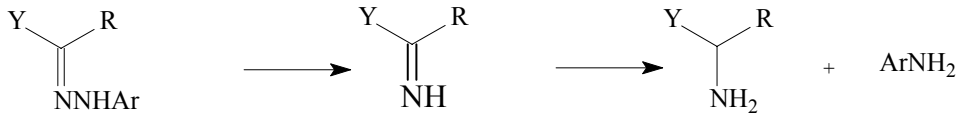


16 **182** **183**

Scheme 50

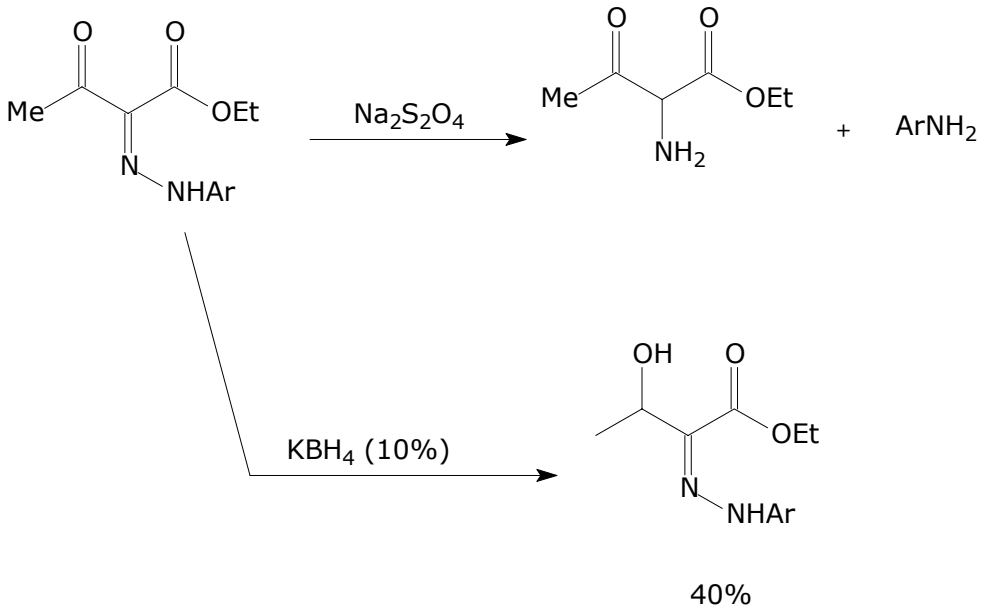
6. Reduction

Reduction of arylhydrazone **16** at dropping mercury electrode proceeds in two successive 2e processes. Initially reductive cleavage of N-N bond occurs. This is followed by 2e reduction of C=NH yielding pi-functionally substituted amines. Again we believe that these results need to be rechecked as functional amines are unstable compounds and although may be formed in solution isolated products should be carefully identified by modern tools.[229]



Scheme 51

The arylhydrazone moiety in **16** is reduced by sodium dithionate into aromatic amine and an α-amino ester. While in potassium borohydride (10%) reduction of carbonyl group was occurred (cf. Scheme 52).[230,231]



Scheme 52

7. References

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Authors

Abdel-Zaher A. Elassar was born in 1960 in Monoufia, Egypt. He received his BSc in chemistry (First class Honors with Distinction from Monoufia University, Egypt, in 1982. Both MSc (Organic Synthesis) and PhD (Organic Polymer Chemistry) were received from Helwan University, Cairo, Egypt, 1988 and 1993, respectively. He was promoted to the rank of associated professor in 2000. He worked at the National Center of Radiation Research and Technology, Cairo, Egypt (1983) and moved in the same year to the Chemistry Department, Helwan University, Cairo, Egypt, where he stayed until 1993. He joined the Chemistry Department, Kuwait University in 1993. His biographical profile was selected for inclusion in the 6th Edition of Who's Who in Science and Engineering, USA. His research interests include organic synthesis, with emphasis on the design and synthesis of new ring system of azoles and azines and the study of their biological activity; organic polymers, concentrated on the modification of the polymeric material for novel synthesis, and use of polymers for waste treatment via metal-complexation.

Hicham H. Dib was born in Lebanon in 1972, and obtained BSc. in Chemistry in 1995 from the Faculty of Science at Beirut Arab University, Beirut, Lebanon, and BS.c of Information (Audio-Visual) in 2001 from the Lebanese University, Lebanon. He obtained MSc. in Chemistry in 2002 from the Faculty of Science at University of Kuwait, Kuwait. Currently, he is a Ph.D candidate and Teaching Assistant at Kuwait University. He was awarded Faiza Al-Khrafi Prize of Scientific Distinction for Graduate Students in June, 2004. He has more than 15 publications.

Nouria Al-Awadi was born in Kuwait and obtained her B.Sc. from the Faculty of Science at Kuwait University in 1976 and Ph.D. from the University of Kent, UK, in 1979. She held a postdoctoral fellowship at the University of Sussex (1981–82). Prof. Al-Awadi is FRCS and chartered scientist of RSC. She has been professor of organic chemistry at the University of Kuwait since 1992. Prof. Al-Awadi has held several administrative positions at Kuwait University: Vice dean of the College of Graduate Studies at Kuwait University (1984–90); Head of the Chemistry Department (1992–95); dean of Faculty of Science (1995–2001); Prof. Al-Awadi since September 2006 until now is vice-president of Kuwait University for academic affairs. Prof. Al-Awadi has specialized in studying kinetics and mechanisms of gas-phase reactions and their potential utility as green methodologies in organic chemistry. She has more than 95 published papers and one patent. She is author of three review articles.

Mohamed Hilmy Elnagdi was born in Egypt in September 1941. He graduated from the Faculty of Science at Cairo University in 1962; since that date, Prof. Elnagdi has worked at Cairo University, Faculty of Science, in the Chemistry Department. Prof. Elnagdi obtained his M.Sc. in 1966, Ph.D. in 1969, and D.Sc. in 1982. He has also been awarded a Diploma in Applied Chemistry from Tokyo Institute of Technology in 1973. Prof. Elnagdi has been professor of organic chemistry at Cairo University since 1980. He worked as professor of organic chemistry at Kuwait University from 1993 to 1999, then as visiting professor at the same university in 2003.

Since March 2007 Prof. Elnagdi has shifted back to the University of Kuwait with intention to end his career there. Prof. Elnagdi has received fellowships from several institutions, including those from the Royal Norwegian Council for Scientific and Industrial Research, taken at University of Oslon (1977); Visiting Associate Professor at the University of Utah in 1976 with Prof. L. B. Townsend; Alexander von Humboldt Fellowship at University of Bonn with Profs. H. Wamhoff and R. Regitz. The Alexander von Humbolt Foundation has continually supported his activities in Germany, enabling him to cooperate with many German colleagues including Profs. K. Hafner, K. S. Hartki, M. Hoffmann, and H. H. Otto. Prof. Elnagdi has specialized in the synthesis of polyfunctional heterocycles and has published around 300 papers in this area as well as 15 review articles. In addition, Prof. Elnagdi is cooperating with the Al-Awadi group at Kuwait University, where he is co-author on 30 papers. He has received several national and regional awards for his research output, including the TWAS Chemistry and COMESTECH awards.