Egypt. J. Chem. **54**, No. 6, pp. 703-721 (2011)

Studies on Substituted Heteroarenes: New Synthesis of Substituted Pyrrole, Pyridine, Pyrazolo[4,3-*b*pyridine, Pyrano [3,2-*c*]quinoline, Benzo [*f*] chromene, Benzo[*h*] chromene, Chromeno [8,7-*h*]chromene, Chromeno[6,5-*f*] chromene and 2*H*-chromene Derivatives

F.M.A. El-Taweel*, A.A. Elagamey and Sh.M. Elmougy
Department of Chemistry , Faculty of Science , Damietta University, New Damietta City , Egypt.

SEVERAL new pyrazolo[4,3-*b*] pyridines (7a,b) were prepared by reacting arylmethylenenitriles (1a,c or 1i,j) with 4-nitrosoantipyrine (4). Reacting 1a,b,d with 4-azidomethylcarbonylantipyrine 8 gave 2-aminopyrrole (14). Pyrano[3,2-c] quinolines (20a,b and 23) were obtained by reacting 4-hydroxyquinoline (15) with 1g, h;2b, respectively.Reaction of 1 with naphthalenediols 24,27 and 29 yield naphthodipyrans 26a,b,28a,b and 30a,b, respectively. Spironaphthodipyrans (32,33) and spironaphthopyrans (36,37) were prepared through reaction of 2a with naphthalenediols (24,27,34 and 35), respectively. Condensation of thioxothiazole (38) with 3,5-dibromo-2-hydroxybenzaldehyde gave 2*H*-chromene-3-carboxamide (42). 38 also reacted with 1c and 2a to gave 3,5-dicyanopyridines (45 and 47), respectively. Reaction of 2-cyano-*N*`-(1-thiophen-2-yl)ethylidene) acetohydrazide (49) with 1a,b afforded 3,5-dicyanopyridines (53).

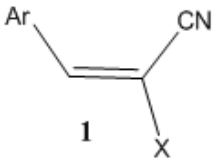
Substituted heteroarenes are interesting as potential biodegradable agrochemicals [1-3], as pharmaceuticals[4], as nonpeptide human deficiency virus (HIV) protease inhibitors[5]antischistosomal agents [6], and antimalarials [7] .

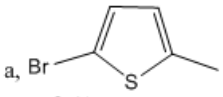
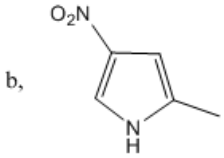
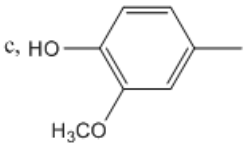
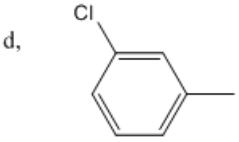
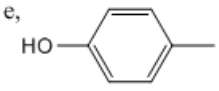
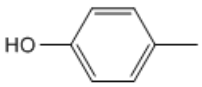
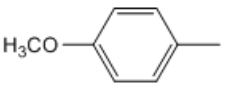
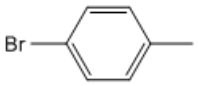
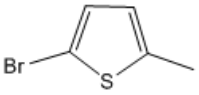
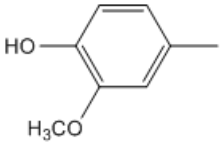
Some years ago, our main interest was focused on a program aimed at developing new synthetic approaches to polyfunctionally substituted heterocycles[8,9] utilizing simple, inexpensive and readily available starting materials.The present work has resulted in the formation of substituted pyrrole, pyridine, pyrazolo[4,3-*b*pyridine, pyrano[3,2-*c*]quinoline, benzo[*f*] chromene, benzo[*h*] chromene, chromeno[8,7-*h*]chromene , chromeno[6,5-*f*] chromene and 2*H*-chromene derivatives.

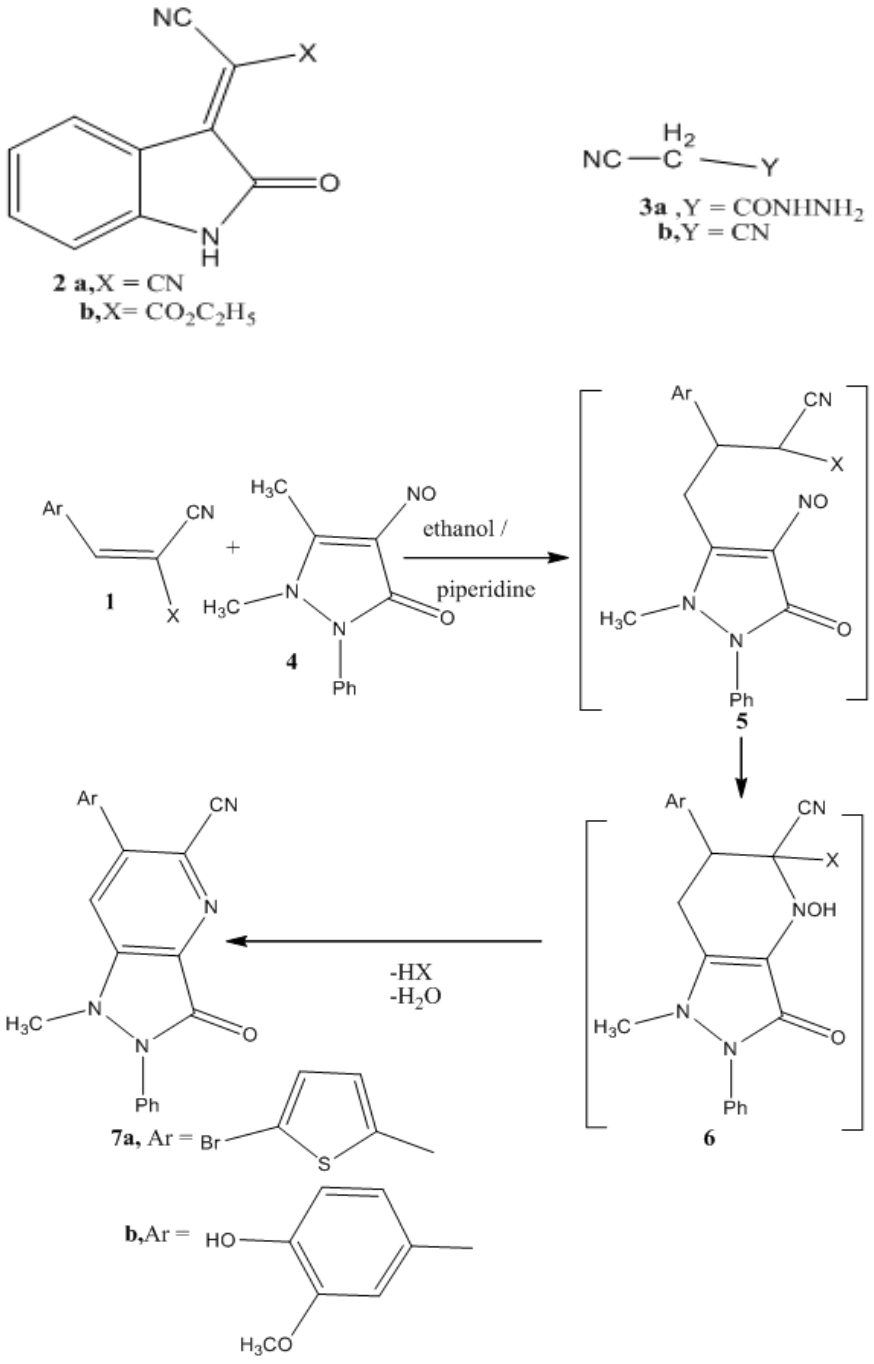
It has been found that, arylmethylenenitriles 1a,c reacted readily with 1,5-dimethyl-4-nitroso-2-phenyl-1*H*-pyrazol-3(2*H*)-one (4) to give 6-aryl-1-methyl-3-oxo -2-phenyl-2,3-dihydro-1*H*-pyrazolo[4,3-*b*]pyridine-5-carbonitriles (7a,b) *via* hydrogen cyanide and water elimination. Structures 7a,b were assigned as

*E.mail:fathyeltaweel@yahoo.com

reaction products based on their elemental and spectral data (*c.f.* Experimental). The same products were obtained by reacting arylmethylenenitriles 1i,j with 4 *via* elimination of one mole of ethyl formate and water. Compounds 7 were assumed to be formed *via* addition of the active methyl group in 4 to the activated double bond in 1 to give the adducts 5 which cyclized to give the intermediates 6. The later aromatized through elimination of hydrogen cyanide or ethyl formate and water. Similar sequence for the formation of similar systems has been reported before [3,7] (*c.f.* Scheme 1).



1	Ar	X
a,		, CN
b,		, CN
c,		, CN
d,		, CN
e,		, CN
f,		, CN
g,		, $CONH_2$
h,		, $CONH_2$
i,		, CO_2H_5
j,		, CO_2H_5


NC
X
O
N
H
2 a,X = CN
b,X= CO2C2H5
H2
NC—C—Y
3a ,Y = CONHNH2
b,Y = CN
Ar
CN
X
1
H3C
NO
N
N
O
Ph
4
ethanol /
piperidine
5
6
NOH
-HX
-H2O
7a, Ar = Br
S
b,Ar = HO
H3CO

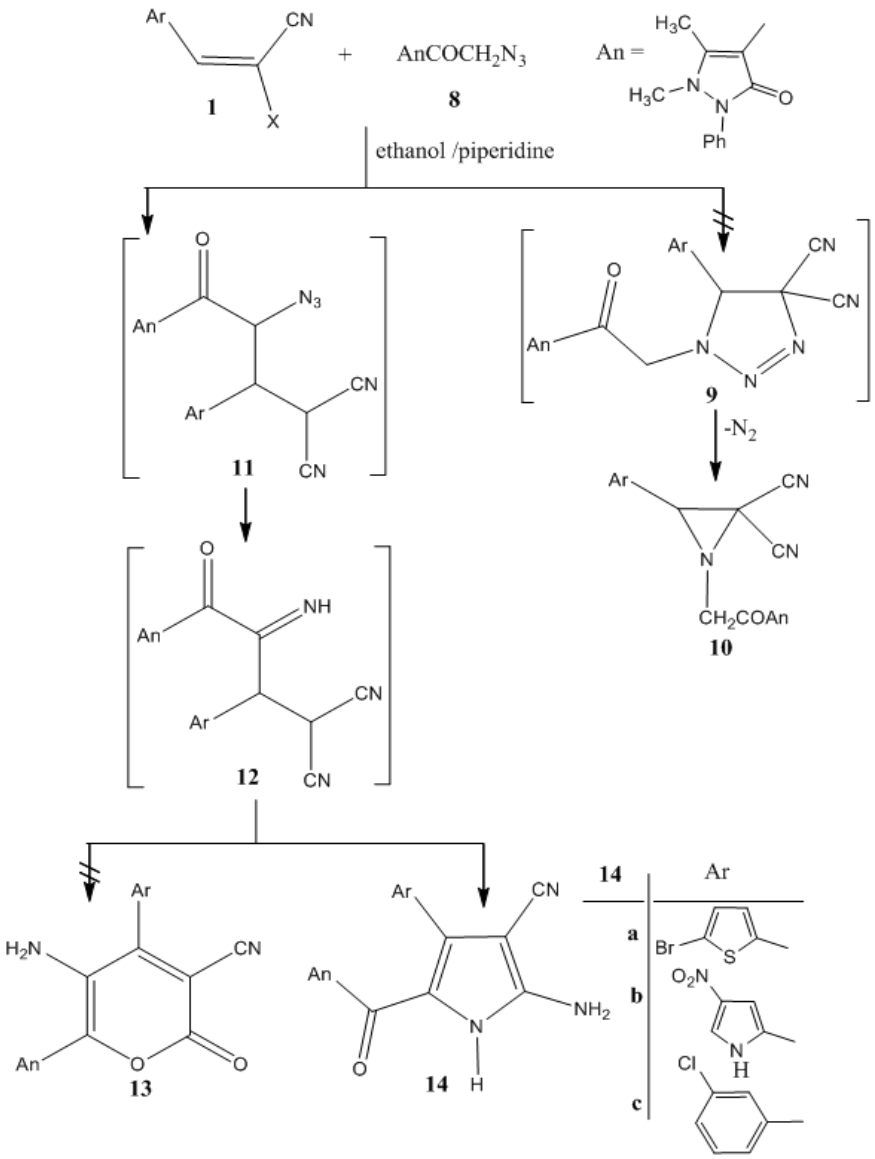
Scheme 1

When equimolecular amounts of arylmethylenenitriles 1a,b,d and 4-azidomethylcarbonyl -1,2-dihydro-2,3-dimethyl -1-phenyl-3-pyrazolin-5-one (8) reacted in ethanolic / piperidine, products resulting *via* elimination of nitrogen from phenylpyrazol-5-oxo-4-yl)-3-arylaziridine-2,2-dicarbonitriles (10), 3-amino-4-(aryl)-6-(2,3-dihydro-1,5-dimethyl-3-oxo-2-phenyl -1*H*-pyrazol-4-yl)-2-oxo-2*H*-pyran-3-carbonitrile (13) and 2-amino-4-aryl-5-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazole-4-carbonyl)-1*H*-pyrrole-3-carbonitriles (14) were thus considered. The aziridine structures (10) were ruled out by ^{1}H-NMR spectra of the reaction products which clearly indicate the absence of methylene groups signals at $\delta \approx 4.0$ ppm . The α-pyrone structures 13 were excluded by IR spectra which clearly indicate the absence of $\upsilon \approx 1700$ cm^{-1} α-pyrone carbonyl function. Thus, the pyrrole structures14a, b were given for the reaction products. Compounds 14 were formed via stepwise mechanism demonstrated in Scheme 2.

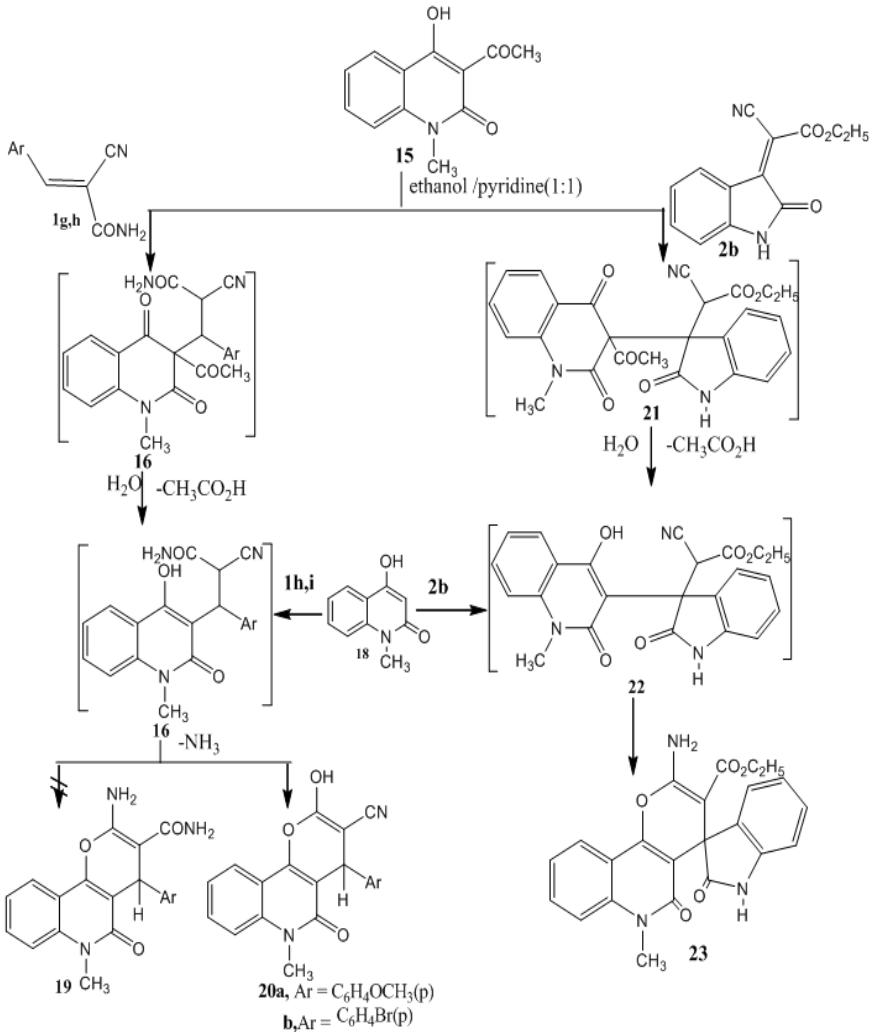
Also, 3-acetyl-4-hydroxy-1-methylquinoline-2(1*H*)-one (15) reacted with arylmethylenenitriles 1g,h in ethanol / pyridine (1:1) to yield 1:1adducts for which two structures; 2-amino-4-aryl-6-methyl-5-oxo-5,6-dihydro 4*H*-pyrano[3,2-*c*] quinolin-3-carboxamides (19) and 2-amino-4-aryl-6-methyl-5-oxo-5,6-dihydro 4*H*-pyrano[3,2-*c*]quinolin-3-carbonitriles (20a,b) seemed possible. Structures 20 were established for the reaction products based on the elemental analysis and IR spectral data which showed signals at ($\upsilon_{CN} \approx$ 2200-2206 cm^{-1}). Structure 20 was also supported through the formation from reaction of 4-hydroxy-1-methylquinolin-2(1*H*)-one (18) with 1g,h utilizing the same reaction conditions.Compounds (20a,b) were proposed to be formed *via* the stepwise mechanism (*c.f.*Scheme 3).

Similarly, compound 15 reacted with ethyl 2-(2-oxoindolin-3-ylidene) cyanoacetate (2b) to yield ethyl 2^{-}-amino-6^{-}-methyl-2,5^{-}-dioxo-5^{-}-,6^{-}-dihydrospiro[indoline-3,4^{-}- pyrano[3,2-*c*]quinolin]-3^{-}-carboxylate (23). Compound 23 was authentically prepared *via* reaction of 2b with 4-hydroxy- 1-methylquinolin-2(1*H*)-one (18) using the same reaction conditions (*c.f.* Scheme 3) .

The behavior of several napthalenediols towards arylmethylenenitriles 1 was investigated. Thus, it has been found that, arylmethylenenitriles 1 reacted readily with 1,5-naphthalenediol (24) in a molar ratio (2:1) in refluxing ethanol containing piperidine as catalyst to afford 2:1 diadducts. Two possible isomeric structures 4-amino- 1,5-diaryl-2,5- dihydro -8-hydroxynaphtho[1,2-*b*]pyrano [2,3-*b*`] pyridine-3,3 -dicarbonitriles (25) and 3,9-diamino-1,7-diaryl-1,7-dihydrochromeno[8,7-*h*] chromene -2,8-dicarbonitriles (26a,b). Structures 26a,b were established for the products based on ^{1}H-NMR spectra which revealed the presence of two magnetically equivalent 4*H*-pyran protons at $\delta \approx 5.0$ ppm. The reaction products 25, were excluded due to two magnetically non-equivalent protons for 4*H*-pyran and pyridine H-2.


Ar
CN
X
1
+
AnCOCH2N3
8
An =
H3C
H3C
N
N
O
Ph
ethanol /piperidine
O
An
N3
Ar
CN
CN
11
Ar
CN
CN
O
An
N
N
N
9
-N2
Ar
CN
CN
N
CH2COAn
10
O
An
NH
Ar
CN
CN
12
H2N
Ar
CN
An
O
O
13
Ar
CN
An
O
N
H
NH2
14
14
Ar
a
Br
S
b
O2N
N
H
c
Cl

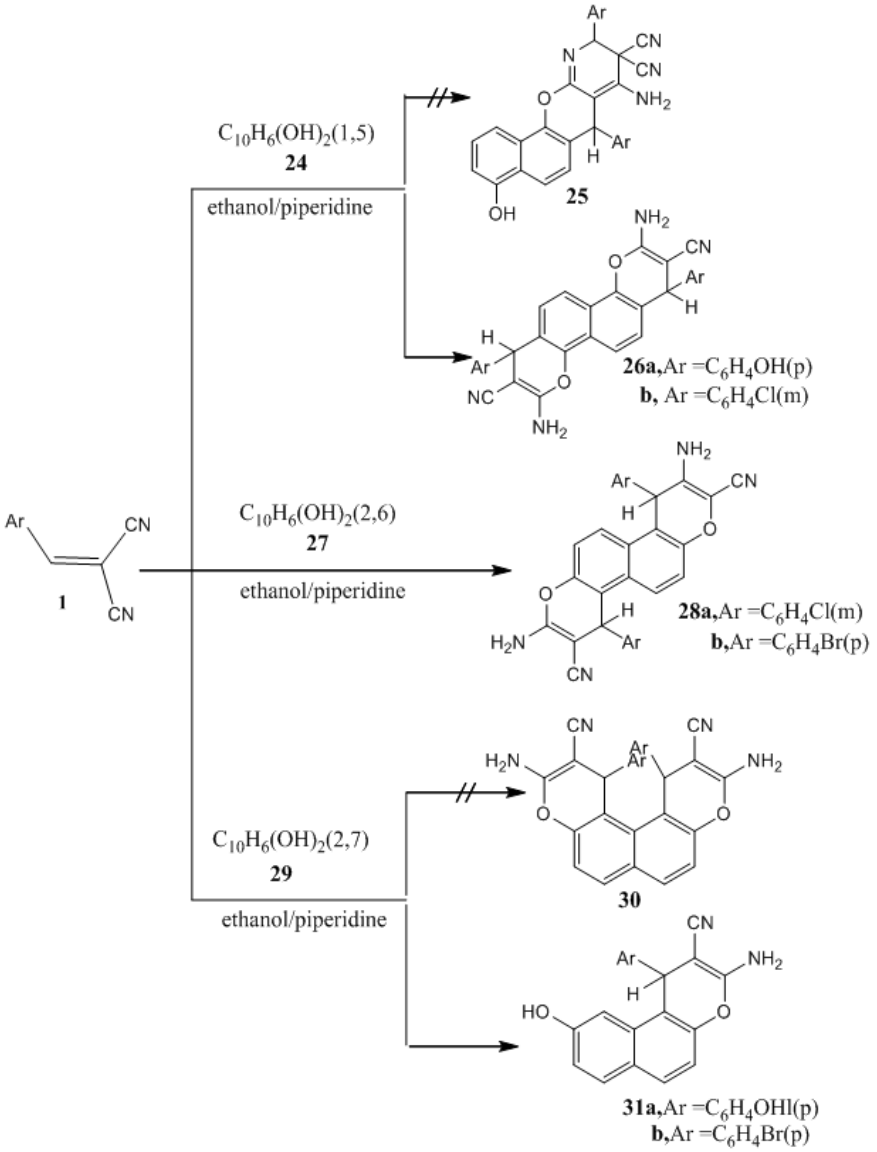
Scheme 2



Scheme 3

Similarly, arylmethylenenitriles 1 reacted with 2,6-naphthalenediol (27) in ethanol catalyzed with piperidine to afford 2:1diadducts which correspond to 3,8- diamino- 4,10- diaryl- 4,10- dihydrochromeno [6,5-*f*] chromen e-2,9 dicarbonitriles (28). Trials to isolate a 1:1 adduct failed. ^{1}H-NMR spectra of 28 revealed the presence of two magnetically equivalent 4*H*-pyran protons as one signal at $\delta \approx 5.34$ ppm. It is of value to note that the pyran *H*-4 in 28 is deshielded by 0.34 ppm in comparison with 26 as a result of van der Waal`s effect of the adjacent aromatic protons (*c.f.* Experimental).

Also, compound 1 reacted with 2,7-naphthalenediol (29) in ethanol and in the presence of piperidine as catalyst to afford the adducts correspond to 3-amino-1-aryl-9-hydroxy-1*H*-benzo[*f*]chromen-2-carbonitriles (31a,b).Structures 31a,b were preferred over possible naphthodipyrans (30) on the basis of elemental and spectral analysis . Also, structure 31 were found to be highly sterically hindered by the two aryl groups at C-1 and C-12. Trials to isolate a 2:1 diadducts 30 were found unsuccessful (*c.f.* Scheme 4).



Scheme 4

Reaction of 2-(2-oxoindolin-3-ylidene) malononitrile (2a) with 1,5-naphthalenediol (24) and 2,6-naphthalenediol (27) in ethanol containing few drops of piperidine afforded a 2:1 diadducts. Structures 2,8-diamino- 4,10-di [1`,3`-dihydro-2`*H*-indol-2-on) spiro]naphtha [1,2-b:5,6-b`] dipyran-3,9-dicarbonitrile (32) and 3,9-diamino-1,7-di[1`,3`-dihydro-2`*H*-indol-2-on) spiro]naphtha [2,1-*b*:6,5-*b*`] dipyran-2,8-dicabonitrile (33) were assigned for the reaction products based on their elemental and spectral analysis (*c.f.* Experimental).

On the other hand, reaction of both of 1,4-naphthalenediol (34) and 1,6-naphthalenediol (35) with 2-(2-oxoindolin-3-ylidene)malononitrile (2a) in a molar ratio (1:1) or (1:2) in ethanolic-piperidine, resulted in the formation of 2-amino-6-hydroxy-2-oxospiro[benzo[*h*]chromene-4,3'-indoline]-3-carbonitrile(36) and 2-amino-8-hydroxy -2'-oxospiro [benzo[*h*] chromene-4,3'-indoline] -3-carbonitrile (37), respectively (*c.f.*Scheme 5). Elemental and spectral data are compatible with the proposed structures 36,37 (*c.f.* Experimental).

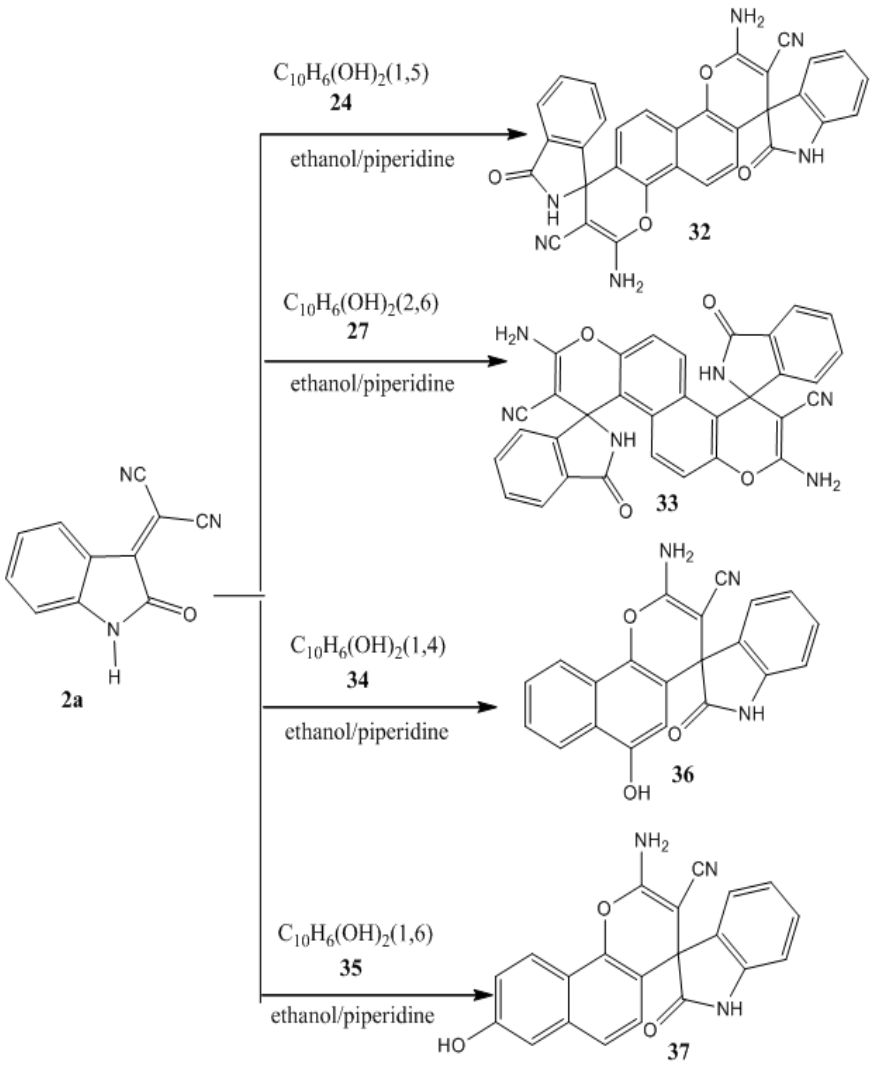
Trials to prepare naphthodipyans *via* reacting 2a with 1,4-naphthalenediol (34) and 1,6-naphthalenediol 35 failed. This many be attributed to the molecular overcrowding arising from the difficult formation of two pyran moieties located at 3,4-,5,6 and 9,10- in positions the naphthalene ring (*c.f.* Scheme 5).

The utility of 2-cyanoacetohydrazide (3a) as starting material for synthesis of heterocyclic compounds was investigated. Thus, treating 3a with carbon disulfide in dimethylformamide under basic conditions in potassium hydroxide / dimethylformamide, followed by reaction with 4-(2-chloroacetyl)1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (38) afforded 2-cyano-*N*-(4-(1,5-dimethyl-3-oxo-2-phenyl -2,3- dihydro -1*H*-pyrazol -4-yl) -2-thioxothiazol -3(2*H*)-yl)] acetamide (39) [(10)] .

We have studied the chemical reactivity of 39 towards different reagents. For example, compound 39 condensed with 3,5-dibromo-2-hydroxybenzaldehyde (40) in ethanol containing catalytic amount of acetic acid to afford 6,8-dibromo-*N*-(4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-2- thioxothiazol-3(2*H*)-yl)- 2-oxo-2*H*-chromene-3-carboxamide (42). Formation of 42 was assumed to proceed *via* the formation of the intermediate arylidene 41, followed cyclization *via* addition of the hydroxyl group to the cyano group and ammonia elimination.

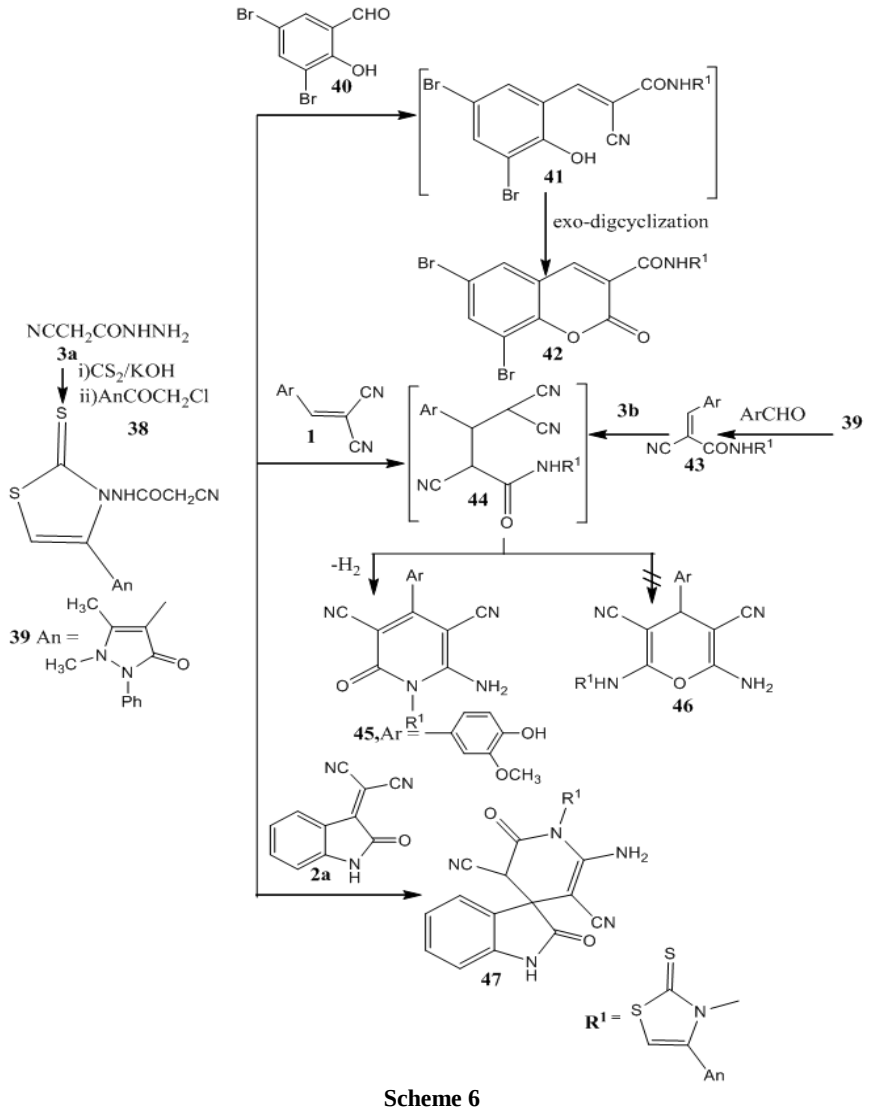
Refluxing 2-cyano- *N*-4-(2,3-dimethyl -1-phenyl-3-pyrazolin -5-on-4-yl) -2-thioxothiazol-3-yl)]acetamide (39) with the arylmethylenenitriles 1 in ethanol containing catalytic amount of triethylamine resulted in the formation of 6-amino-1-[4`-(2,3-dimethyl-1-phenyl-3-prazolin-5-oxo-4-yl)-2`-thioxothiazol-3`-yl]-4-aryl-3,5-dicyano-2-oxopyridine 45 or the 4*H*-pyran (46). Structures 45 were proposed as reaction products based on their elemental and spectral analysis. If the reaction products are 46, ^{1}H-NMR spectra would show signal

at ≈ 4.5-5.00 ppm for pyran H-4. Moreover, compound 45 was also prepared *via* the reaction of (*E*)-2-cyano-*N*-(4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl) -2-thioxothiazol-3(2*H*)-yl) -3- (4-hydroxy - methoxyphenyl) acrylamide (43)with malononitrile 3b in ethanolic-pyridine. Formation of 45 was suggested to take place *via* Michael type addition of the active methylene group in 39 to the π-deficient centre in 1 to give Michael adduct intermediate 44, which cyclized and readily eliminate of one molecule of hydrogen to yield 45.



Scheme 5

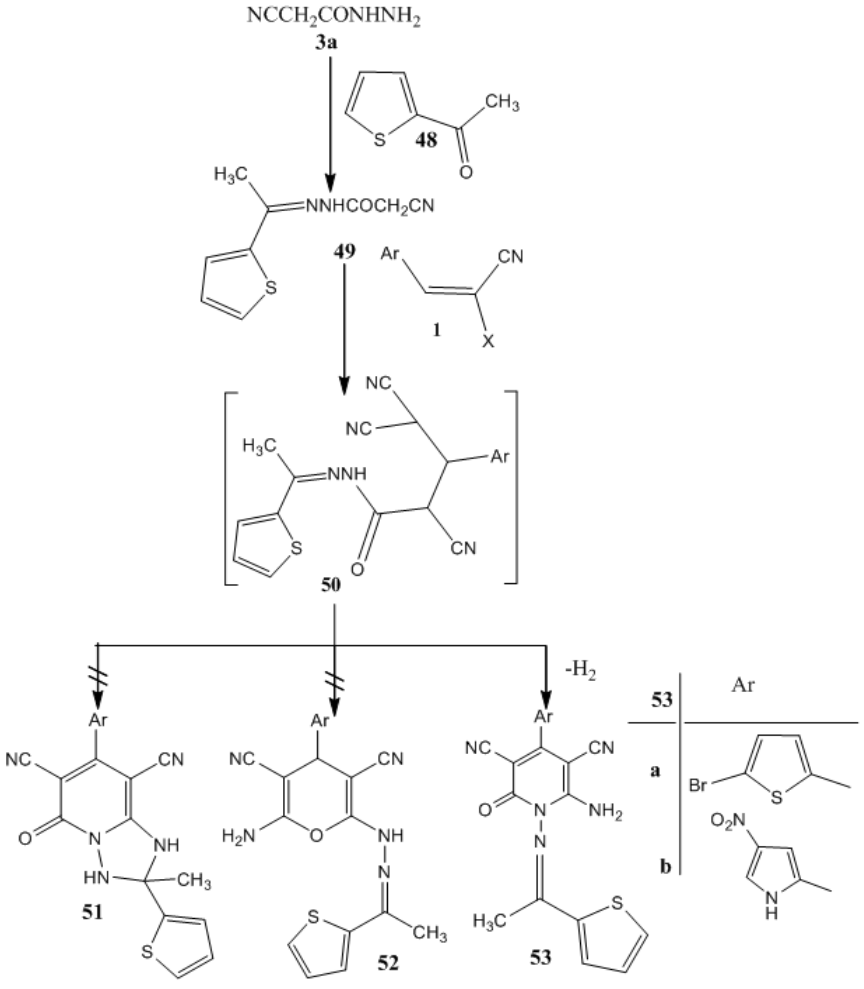
Similarly, compound 39 reacted with 2a to yield 6-amino-1-(4-(1,5-dimethyl-3-oxo -2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl) -2-thioxothiazol-3 (2*H*)-yl) -2,2-dioxo-2,3-dihydro-1 *H*-spiro[indoline-3,4-pyridine]-3,5-dicarbonitrile (47) (*c.f.* Scheme 6).



Scheme 6

Finally,2- cyano- *N*`-(1-thiophen -2-yl) ethylidene) acetohydrazide (49)[11] prepared by condensing 2-cyanoacetohydrazide (3a) with 2-acetylthiophene (48), reacted with the arylmethylenenitriles 1 in ethanol catalyzed by piperidine to give 7-(aryl) -1,2,3,5- tetrahydro-2-methyl-5-oxo-2-(thiophen-2-yl)-[1,2,4] triazolo [1,5-*a*]

pyridine-6,8-dicarbonitriles (51), 2-(2-(1-(thiophen-2-yl) ethylidene)hydrazinyl)-6-amino-4-(aryl)-4*H*-pyran-3,5-dicarbonitrile (52) or 6-amino-4- aryl-3,5- dicyano-1-[1`-(2``-thienyl)ethylidenemino]pyridine-2-(1*H*)-ones (53). Structures 51 excluded by ^{1}H-NMR spectrum which clearly indicates the absence of two singlets due to two NH groups. Also, ^{1}H-NMR spectrum of the products clearly showed the absence of 4*H*-pyran proton at $\delta \approx 4.5$-5.0 ppm for structure 52. Consequently, the pyridine structures 53 were elucidated as reaction products. Compounds 53 were suggested to be obtained *via* the addition of the active methylene group in 49 to the π-deficient carbon in 1 to give the adducts 50 which cyclized and dehydrogenated to give (*E*)-6-amino-4-aryl-2-oxo-1-(thiophen-2-yl)ethylideneamino)-1,2-dihydro pyridine -3,5-dicarbonitriles (53) (*c.f.* Scheme 7).



Scheme 7

Experimental

All melting points are uncorrected and measured on Griffin & George MBF 010T (London) apparatus. Recorded yields correspond to the pure products . IR (KBr) spectra were recorded on a perkin Elmer SP-880 spectrophotometer and ^{1}H-NMR spectra were measured on a Varian 500 MHz at Minnesota (U.S.A.) University spectrometer in DMSO-d $_6$as solvent and TMS as an internal standard (Chemical shifts are reported in δ units ppm). Microanalyses were performed on LECOCHN-932 and carried out in the Microanalytical Data Units at Cairo and Mansoura University.

Synthesis of 6-aryl-1-methyl-3-oxo -2-phenyl-2,3-dihydro-1H-pyrazolo[4,3-b] pyridine-5-carbonitriles (7a,b)

A solution of 1,5-dimethyl-4-nitroso-2-phenyl-1*H*-pyrazol-3(2*H*)-one (4) (0.01 mol) and the arylmethylenenitriles 1a,c or 1i,j (0.01 mol) in ethanol (50 ml) containing a catalytic amount of piperidine (0.1 ml) was heated under reflux for 1hr, then left to cool. The solid products so formed were collected by filtration, recrystallized from the suitable solvents and then identified as 7a,b.

6-(5-Bromothiophen-2-yl)- 1-methyl-3-oxo- 2-phenyl -2,3-dihydro -1H-pyrazolo[4,3-b]pyridine-5-carbonitrile (7a)

Yellow crystals from ethanol / DMF, m.p. 240-242 °C, yield 80%.- IR (υ_{max} / cm^{-1}) : 2225 (conjugated CN), 1691 (CO). ^{1}H-NMR (DMSO-d_6) (δ, ppm) : 3.35 (s, 3H, N-CH_3), 6.97-7.59 (m, 7H, aryl H), 8.37 (s, 1H, pyridine H-4). $C_{18}H_{11}BrN_4SO$ (411.28) Calcd. C 52.57 H 2.70 N 13.62 ; Found C 52.36 H 3.04 N 13.50.

6-(4-Hydroxy-3-methoxyphenyl)- 1-methyl-3-oxo- 2-phenyl -2,3-dihydro -1H-pyrazolo[4,3-b]pyridine-5-carbonitrile (7b)

Red crystals from ethanol, m.p. 260-262 °C, yield 77 %. -IR (υ_{max} / cm^{-1}) : 3065 (br, OH), 2224 (conjugated CN), 1661 (CO).- ^{1}H-NMR (DMSO-d_6) (δ, ppm) : 3.4 (s, 3H, N-CH_3), 3.87 (s, 3H, OCH_3), 6.97-7.59 (m, 8H, aryl H), 8.37 (s, 1H, pyridine H-4), 9.64 (s, 1H, OH). $C_{21}H_{16}N_4O_3$ (372.38) Calcd. C 67.73 H 4.33 N 15.05 ; Found C 67.64 H 4.4 N 15.13.

2-Amino-4-aryl-5-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carbonyl)-1H-pyrrole-3-carbonitriles (14a-c)

A solution of 4-azidmethylcarbonyl-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one (8) (0.01 mol) and the appropriate amounts of 1a,b,d (0.01 mol) in ethanol (50 ml) was heated with piperidine (0.1 ml) under reflux for 1hr, then left to cool at room temperature. The solid products, so formed, were collected by filtration, recrystallized and identified as 14a-c.

2-Amino -4- (5-bromothiophen-2-yl) -5(-1,5-dimethyl -3-oxo -2-phenyl -2,3-dihydro-1H-pyrazole-4-carbonyl)-1H-pyrrole-3-carbonitrile (14a)

Yellow crystals from ethanol /1,4-dioxan, m.p. 286-288 °C, yield 60 %- IR (υ_{max} / cm^{-1}) : 3470, 3360 (NH_2, NH), 2203 (conjugated CN), 1685 (CO), 1650 (CO). - ^{1}H-NMR (DMSO-d_6) (δ, ppm) : 2.40 (s, 3H, CH_3), 3.33 (s, 3H, N-CH_3), 7.45-7.63 (m, 9H, 7H, aryl H and 2H, NH_2), 8.5 (s, 1H, NH).- $C_{21}H_{16}BrN_5SO_2$ (482.37) Calcd. C 52.29 H 3.34 N 14.52 ; Found C 52 . 12H 3.51 N 14.63.

2-Amino-4-(4-nitropyrrol-2-yl)-5(-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carbonyl)-1H-pyrrole-3-carbonitrile (14b)

Brown crystals from DMF, m.p. 263-265 °C, yield 60 %.- IR (υ_{max} / cm^{-1}) : 3452, 3358, 3137 (NH_2, NH), 2191 (conjugated CN), 1680 (CO), 1660(CO). ^{1}HNMR : Insoluble .$C_{24}H_{21}N_5O_4$ (443.45) Calcd.C 65.00 H 4.77 N 15.79 ; Found C 65.12 H 5.00 N 15.68 .

2-Amino-4-(3-chlorophenyl)-5(-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carbonyl)-1H-pyrrole-3-carbonitrile (14c)

Yellow crystals from ethanol / 1,4-dioxan , m.p. 284-286 °C, yield 65%.- IR(υ_{max} / cm^{-1}) : 3441, 3341 (NH_2, NH), 2203 (conjugated CN), 1685 (CO), 1620 (CO).. $C_{23}H_{18}ClN_5O_2$ (431.87) Calcd.C 63.96 H 4.20 N 16.22 ; Found C 63.89 H 4.31 N16.14.

Synthesis of 2-amino-4-aryl-6-methyl-5-oxo-5,6-dihydro 4H-pyrano[3,2-c]quinolin-3-carbonitriles (20a,b) and spiro-4H-pyrano[3,2-c]quinolin-3-carboxylate (23)

A solution of 3-acetyl-4-hydroxy-1-methylquinoline-2(1*H*)-one (15) (0.01 mol) and (0.01 mol) of either 1g,h or ethyl 2-(2-oxoindolin-3-ylidene) cyanoacetate (2b) in ethanol-pyridine (1:1) (60 ml), were refluxed for 6 hr. The solvent was then evaporated in *vacuo* and the precipitates formed were collected by filtration recrystallized and identified as 20a,b and 23, respectively.

2-Amino-4-(4-methoxyphenyl)-6-methyl-5-oxo-5,6-dihydro 4H-pyrano[3,2-c] quinolin-3-carbonitriles (20a)

Colorless crystals from ethanol, m.p. 190-192 °C, yield 70%.-IR (υ_{max} / cm^{-1}) : 3447, 3366, 3304 (OH), 2206 (conjugated CN), 1699 (CO). -^{1}HNMR : (DMSO-d_6) (δ, ppm) :3.10(s,3H,CH_3),3.83(s,3H,CH_3),4.43(s,1H,pyran H-4),6.90-8.16(m,8H,aryl H).- $C_{21}H_{16}N_2O_4$ (360.36) Calcd.C 69.99H, 4.48 N 7.77 ; Found C 70.02 H 4.73 N 7.68.

2-Amino-4-(4-bromophenyl)-6-methyl-5-oxo-5,6-dihydro 4H- pyrano [3,2-c] quinolin-3-carbonitriles (20b)

Faint yellow crystals from ethanol / DMF, m.p. 220-222 °C, yield 80 %.-IR (υ_{max} / cm^{-1}) : 3451, 3409, 3325 (OH), 2200 (conjugated CN), 1682 (CO). -^{1}HNMR : (DMSO-d_6) (δ, ppm) :3.0(s,3H,CH_3),4.50(s,1H,pyran H-4),7.35-8.16(m,8H,aryl H) .- $C_{20}H_{13}BrN_2O_3$ (409.23) Calcd. C 58.70 H 3.20 N 6.85 ; Found C 58.65 H 3.34 N 6.80.

Ethyl2′-amino-6-methyl-2,5′-dioxo-5′-,6′-dihydrospiro[indoline-3,4¯pyrano [3,2-c] quinolin]-3-carboxylate (23)

Yellow crystals from ethanol / DMF, m.p. 270-272 °C, yield 70%.-IR (υ_{max} / cm^{-1}) : 3395, 3284, 3196 (NH_2 ,NH), 1688 (CO), 1659 (CO), 1631 (CO). -^{1}HNMR : (DMSO-d_6) (δ, ppm) : 0.82-0.85 (t, J=7.5Hz, 3H, CH_3), 2.87(s, 3H, CH_3), 3.73-3.76 (q, J=7.5Hz, 2H, CH_2), 6.69-8.14(m, 10H, 8H, aryl H and 2H, NH_2), 10.28 (s, 1H, NH).- $C_{23}H_{19}N_3O_5$ (417.41) Calcd. C 66.18 H 4.59 N 10.07 ; Found C 66.22 ;H 4.33 N 10.13.

General procedure for preparation of (26a,b), (28a,b) and (31a,b)

A mixture of (0.01 mol) of each 1,5-naphthalenediol (24), 2,6-naphthalenediol (27) or 2,7-naphthalenediol (31) and (0.02 mol) of the arylmethylenenitriles 1 in ethanol (50 ml) was refluxed for 30 min, in the presence of piperidine (0.1 ml). The obtained solid products were collected by filtration and recrystallized from the proper solvents yielding corresponds compounds 26, 28 and 31, respectively.

3,9-Diamino- 1,7-di (4-hydroxyphenyl) -1,7- dihydrochromeno [8,7-h] chromene -2,8-dicarbonitrile (26a)

Yellow crystals from ethanol / DMF, m.p., >300 °C, yield 65%. -IR (υ_{max} / cm^{-1}) : 3421, 3321 (NH_2, OH), 2187 (conjugated CN), 1653 (δNH_2). -^{1}H-NMR (DMSO-d_6) (δ, ppm) : 4.77(s, two equivalent pyran 4-H), 6.69-7.88 (m, 16H, 12H, aryl H and 4H, 2NH_2), 9.32 (s, 2H, 2OH).- $C_{30}H_{20}N_4O_4$ (500.50) Calcd. C 71.99 H 4.03 N 11.19 ; Found C 71.03 H 4.34 N 11.22.

3,9-Diamino-1,7-di(4-bromophenyl) -1,7-dihydrochromeno[8,7-h] chromene -2,8-dicarbonitrile (26b)

Yellow crystals from DMF, m.p., > 300 °C, yield 63%.-IR (υ_{max} / cm^{-1}) : 3499, 3325, 3197 (NH_2), 2196 (conjugated CN), 1665 (δ NH_2). $C_{30}H_{18}Cl_2N_4O_2$ (537.39) Calcd. C 67.05 H 3.38 N 10.43 ; Found C 67.23 H 3.42 N 10.33.

3,8-Diamino-4,10-di(4-chlorophenyl)-4,10-dihydrochromeno[6,5-f]chromene -2,9- dicarbonitriles (28a)

Yellow crystals from DMF m.p. > 300 °C, yield 64 %. – IR: (υ_{max} / cm^{-1}) : 3458, 3326, 3199 (NH_2), 2193 (conjugated CN), 1657 (δ NH_2). $C_{30}H_{18}Cl_2N_4O_2$ (537.39) Calcd.C 67.05H 3.38 N 10.43 ; Found C 67.00 H 3.27 N 10.51.

3,8-Diamino- 4,10- di(4-bromophenyl)- 4,10- dihydrochromeno [6,5-f] chromene-2,9-dicarbonitriles (28b)

Faint yellow from ethanol / DMF m.p. >300 °C, yield 65 %.- IR (υ_{max} / cm^{-1}) : 3457, 33327, 3197 (NH_2), 2191 (conjugated CN).- ^{1}H-NMR (DMSO-d_6) (δ, ppm) : 5.34 (s, two equivalent pyran 4-H), 6.99-7.89 (m, 16H, 12H, aryl H and 4H, 2NH_2). $C_{30}H_{18}Br_2N_4O_2$ (626.29) Calcd. C57.53 H 2.90 N 8.95 ; Found C 57.64 H 3.02 N 8.83.

3-Amino -9- hydroxyl -1- (4-hydroxyphenyl) -1H-benzo [f] chromen-2-carbonitrile (31a)

Yellow crystals from ethanol / DMF, m.p. 260-262 °C, yield 70%.-IR (υ_{max} / cm^{-1}) : 3482, 3377, 3162 (NH_2, OH), 2183 (conjugated CN), 1651 (δ, NH_2). -^{1}H-NMR (DMSO-d_6) (δ, ppm) : 4.89 (s, 1H, pyran 4-H), 6.65-7.77 (m, 11H, 9H aryl H and 2H, NH_2), 9.26,9.8 (2s, 2H, 2OH). $C_{20}H_{14}N_2O_3$ (330.33) Calcd.C 72.72 H 4.27 N8.48 ; Found C 72.82 H 4.15 N 8.51 .

3-Amino-9-hydroxy-1-(4-bromophenyl)-1H-benzo[f]chromen-2-carbonitrile (31b)

Yellow crystals from DMF, m.p. 268-270 °C, yield 70 %. IR (υ_{max} / cm^{-1}) : 3480-3338 (NH_2, OH), 2189 (conjugated CN), 1648 (δ NH_2). ^{1}H-NMR: Insoluble . $C_{20}H_{13}BrN_2O_2$ (393.23) Calcd. C 61.09 H3.33 N 7.12 ; Found C 61.32 H 3.51 N7.30 .

Synthesis of compounds 32 and 33

Genaral procedure

A suspension of (0.01 mol) of each of 1,5-naphthalenediol (24) or 2,6-naphthalenediol (27) and 2-(2-oxoindolin-3-ylidene)malononitrile (2a) (0.02 mol) in ethanol (50 ml) containing few drops of piperidine was refluxed for 1 hr. The solids deposited were collected by filtration, recrystallized and identified as 32 and 33, respectively.

2,8-Diamino-4,10-di[1`,3`-dihydro-2`H-indol-2-on)spiro]naphtho [1,2-6:5,6-6`] dipyran-3,9-dicarbonitrile (32)

Yellow crystals from DMF, m.p. >300 °C, yield 75%.-IR (υ_{max} / cm^{-1}) : 3448, 3368, 3313 (NH_2, NH), 2195 (conjugated CN), 1713 (CO), 1655 (δ NH_2).- ^{1}H-NMR (DMSO-d_6) (δ, ppm) : 6.73-7.94 (m, 16H, 12H, aryl H and 4H, $2NH_2$), 10.71 (s, 2H, 2NH). $C_{32}H_{18}N_6O_4$ (550.52) Calcd.C 69.81 H 3.30 N 15.27 ; Found C 69.76 H 3.41 N 15.30

3,9-Diamino-1,7-di[1`,3`-dihydro-2`H-indol-2-on)spiro]naphtho [2, 1-6:6,5-6`] dipyran-2,8-dicabonitrile (33)

Red crystals from ethanol /1,4-dioxan , m.p. 230-232 °C, yield 80%. -IR (υ_{max} / cm^{-1}) : 3405, 3259 (NH_2, NH), 2231 (conjugated CN), 1718 (CO), 1620 (δ NH_2). $C_{33}H_{20}N_6O_4$ (564.54) Calcd. C 70.21 H 3.57 N 14.89 ; Found C 70.10 H 3.44 N 14.78 .

General methods for preparation of 36 and 37

A mixture of each of 1,4-naphthalenediol (34) or 1,6-naphthalenediol (35) (0.01 mol) in ethanol (50 ml) containing piperidine (0.1 ml) was treated with (0.01 mol) of 2a. The reaction mixture was refluxed for 6 hr and then left to cool at room temperature. The precipitates formed were collected by filtration, recrystallized and identified as naphthopyrans 36 and, 37, respectively.

2-Amino -6-hydroxy -2¯oxospiro [benzo [h] chromene -4,3- -indoline]-3-carbonitrile (36)

Brown crystals from ethanol/DMF, m.p. > 300 °C, yield 70%.- IR (υ_{max} / cm^{-1}) : 3423, 3301, 3200 (NH_2, NH, OH), 2219 (conjugated CN), 1721 (CO), 1646 (δ NH_2). $C_{21}H_{13}N_3O_3$ (355.34). Calcd. C 70.98 H 3.69 N 11.83 ; Found C 70.62 H 3.53 N 11.69.

2-Amino-8-hydroxy-2'-oxospiro [benzo [h]chromene -4,3- -indoline] -3-carbonitrile (37)

Colorless crystals from ethanol / 1,4-dioxan , m.p. >300 °C, yield 65%. - IR (υ_{max} / cm^{-1}) : 3482, 3328, 3171 (NH_2, NH, OH), 2199 (Conjugated CN), 1699 (CO), 1653 (δ NH_2).- ^{1}H-NMR (DMSO-d_6) (δ, ppm) : 6.43-6.45 (d, J= 9 Hz, 1H, aryl H), 6.96-7.28(m, 7H, aryl H), 7.41(s, 2H, NH_2), 8.13-8.14 (d, J= 9Hz, 1H, aryl H), 10.05 (s, 1H, OH), 10.65 (s, 1H, NH). $C_{21}H_{13}N_3O_3$ (355.34) Calcd.C 70.98 H 3.69N 11.83; Found C 70.88 H 3.76 N 11.75.

6,8-Dibromo -N- (4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-thioxothiazol-3(2H)-yl)-2-oxo-2H-chromene-3-carboxamide (42)

A solution of (0.01 mol) of thiazole derivative 39 and (0.01 mol) of 3,5-dibromo-2-hydroxybenzaldehde (40) in ethanol (50 ml) containing acetic acid (1 ml) was refluxed for 1 hr, then left to cool. The formed precipitate was collected by filtration, recrystallized from ethanol to give 42 as colorless crystals, m.p. 194-196 °C, yield 85 %.- IR (υ_{max} / cm^{-1}) : 3400, 3061 (NH), 1729 (CO coumarinyl), 1660 (CO antipyrinyl). $C_{24}H_{16}Br_2N_4S_2O_4$ (648.34) Calcd.C 44.46 H 2.49 N 8.64 ; Found C 44.69 H 2.53 N 8.55.

(E)-2-cyano-N-(4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-thioxothiazol-3(2H)-yl)-3-(4-hydroxy-3-methoxyphenyl)acrylamide (43)

A solution of thiazole 39 (0.01 mol) and the appropriate amount of aromatic aldehyde (0.01 mol) in ethanol (50 ml) containing (0.1 ml) of piperidine was refluxed for 3 hr, then left to cool. The resulting solid obtained on standing was collected by filtration and recrystallized from ethanol to give 43 as colorless crystals, m.p. 258-260 °C, yield 60%.- IR (υ_{max} / cm^{-1}) : 3250 (NH, 2214 conjugated CN), 1634 (CO antipyrinyl). $C_{25}H_{21}N_5S_2O_4$ (519.59) Calcd. C 57.79 H 4.07 N 13.48 ; Found C57.82 H 4.34 N 13.54.

6-Amino-1- (4-(1,5-dimethyl -3-oxo-2-phenyl -2,3-dihydro -1H-pyrazol-4-yl)-2-thioxothiazol -3(2H)-yl) -4-(4-hydroxy -3-methoxyphenyl) -2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (45)

Method A

A solution of thiazole 39 (0.01 mol) in ethanol (50 ml) containing (0.1 ml) of triethyl amine, was treated with (0.01 mol) of cinnamonitrile 1c. The reaction mixture was refluxed for 3 hr, then left to cool. The solid product formed was collected by filtration and recrystalized from ethanol to give colorless crystals of 45 m.p., 290-292 °C, yield 65%.

Method B

A suspension of the arylidene 43 (0.01 mol) in ethanol (50 ml) was treated with malononitrile (0.01 mol) and dry pyridine (20 ml). The reaction mixture was refluxed for 5 hr and the solvent was concentrated in *vacuo* and the solid formed was recrystallized and identified (m.p. and mixed m.p. as 45). -IR (υ_{max} / cm^{-1}) : 3323, 3198 (NH_2, NH), 2215 (conjugated CN) , 1636 (CO antipyrinyl).). $C_{29}H_{23}N_7S_2O_4$ (597.66) Calcd.C 58.28 H 3.88 N 16.40 ; Found C 58.11 H 4.00 N 16.32.

Formation of 6′-amino -1′- (4-(1,5-dimethyl -3-oxo -2-phenyl-2,3- dihydro-1H-pyrazol-4-yl) -2-thioxothiazol -3(2H)-yl) -2,2¯dioxo -2′,3′-dihydro-1H-spiro [indoline -3,4′ -pyridine] -3′,5′-dicarbonitrile(47)

To a mixture of thiazole 39 (0.01 mol) and 2-(2-oxoindolin-3-ylidene) malononitrile (2a) (0.01 mol) in ethanol (50 ml), few drops of piperidine was added. The reaction mixture was refluxed for 4 hr, then cooled and the formed precipitate was collected by filtration and recrystallized from ethanol / DMF to give red crystals of 47, m.p. 192-194 °C, yield 70%. -IR (υ_{max} / cm^{-1}) : 3250, 3063 (NH), 1723 (CO), 1641 (CO antipyrinyl). $C_{28}H_{20}N_8S_2O_3$ (580.64) Calcd. C 57.92 H 3.47 N 19.30 ; Found C 57.81 H 3.55 N 19.11.

Preparation of (E)-6-amino-4-aryl-2-oxo-1-(thiophen-2-yl)ethylideneamino)-1,2-dihydropyridine-3,5-dicarbonitriles (53a,b)

A solution of the hydrazone derivative 49 (0.01 mol) and (0.01 mol) of arylmethylenenitriles 1a,b in ethanol (50 ml) was heated at reflux temperature for 30 min. The resulting solids were collected by filtration and recrystallized from suitable solvents to yield compounds 53a,b.

(E)-6-amino-4-(5-bromothiophen-2-yl)-2-oxo-1-(thiophen-2-yl) ethylidene amino) -1,2-dihydropyridine-3,5-dicarbonitriles (53a)

Yellow crystals from ethanol / 1,4-dioxan , m.p. 216-218 °C, yield 75%. -IR (υ_{max} / cm^{-1}) : 3451. 3362 (NH_2, NH), 2214 (conjugated CN), 1655 (CO), 1619 (δ NH_2). $C_{17}H_{10}N_7SO_3$ (444.33) Calcd.C 45.95 H 2.27 N 15.76 ; Found C 45.85 H 2.36 N 15.82.

(E)-6-amino-4-(4-nitropyrrol-2-yl)-2-oxo-1-(thiophen-2-yl)ethylideneamino)-1,2-dihydropyridine-3,5-dicarbonitriles (53b)

Colorless crystals from ethanol / DMF, m.p. 248-250 °C, yield 70%.-IR (υ_{max} / cm^{-1}) : 3447, 3320, 3150 (NH_2, NH), 2211 (conjugated CN), 1658 (CO). -^{1}H-NMR (DMSO-d_6) (δ, ppm) : 2.43 (s, 3H, CH_3), 7.09-8.08 (m, 5H, 3H, aryl H and 2H, NH_2), 8.13 (s, 1H, aryl H), 8.35 (s, 1H, aryl H), 12.92 (s, 1H, NH).- $C_{17}H_{11}N_7SO_3$ (393.38) Calcd.C 51.90 H 2.82 N 24.92 ; Found C 51.82 H 2.57 N 24.86.

References

1. **Wellinga, K., Grosscurt, A.C. and Van Hes R.,**1-Phenyl-2-pyrazolines : A new class of insecticides.1.Synthesis and insecticidal properties of 3-phenyl-1-1-phenylcarbamolyl pyrazolines. *J. Agric. Food Chem.* **25** (5) , 987(1977).

2. **Grosscurt, A.C., Van Hes, R. and Wellinga, K.,** 1-Phenyl-2-pyrazolines , a new class of insecticides .3.Synthesis and insecticidal properties of 3,4-diphenyl-1-phenylcarbamolyl pyrazolines. *J.Agric.Food Chem.* **27** (2), 406 (1979).

3. **El-Taweel, F.M.A., Sowellim, S.Z.A. and Elagamey, A.A.,** Studies with polyfunctionally substituted heteroarenes :New synthesis of benzo[c]quinolinones and pyrano [3,2-c] quinoline derivatives. *Boll.Chim. Farm.* **137** , 325(1998).

4. **Tois, J., M., Vahermo, M. and Koskinen, A.,** Novel and convenient synthesis of 4(1*H*) quinolone . *Tetrahedron Lett.* **46**,735 (2005).

5. **Abdelkhalik, M.M., Eltoukhy, A.M., Agamey, S.M. and Elnagdi, M.H.,** Enaminones as building blocks in heterocyclic synthesis : New synthesis of nicotinic acid and thienopyridine derivatives. *J. Heterocycl. Chem.* **41** (3) , 431 (2004).

6. **Othman, E.S.,** Some nucleophilic cyclization reactions with 3-[4-(benzo [1,3] dioxo; ylmethylene) pyrazolyl] quinolone. *Acta Chim. Slov.* **50**, 15 (2003).

7. **El-Taweel, F.M.A., Ibrahim, D.A. and Hanna, M.A.,** Synthesis of some new quinoline derivatives : New routes to synthesize polysubstituted 2(1*H*)-quinolone derivatives. *Boll. Chim. Farm.* **140**, 287 (2001).

8. **El-Taweel, F.M.A.,** Studies with quinolines : New synthetic routes 4*H*, 5*H*, 6*H*,9*H*,-benzo [ij] pyrano [2,3-b] quinolizin-8-one,4H-pyrano [2,3-b] pyridine, 2*H*-pyran-2-one and pyranopyridoquinoline derivatives. *J. Heterocycl . Chem.* **42**, 943(2005).

9. **Elagamey, A.A., El-Taweel, F.M.A. and AbuEl-Enein , R.A.N.,** New synthetic routes to 1,3,4-thiadiazole derivatives. *Phosphorus. Sulfur and Silicon*, **181,** 2155 (2006).

10. **El-Taweel, F.M.A.,** Novel synthesis of thiophene, thiazole, 2*H*-pyran-2-one, benzimidazo [1,2-a] pyridine and pyridine derivatives containing antipyrine moiety. *Phosphorus, Sulfur, and Silicon*,**179**, 1267(2004).

11. **El-Taweel, F.M.A., Sofan, M.A., Abu El-Maati, T.M. and Elagamey, A.A.,** Synthetic routes to fluorenenone , indenopyridine , 4H-naphtho[2,1-b]pyrans and pyridine derivatives. *Boll. Chim. Farm.* **140**, 306 (2001).

(*Received* 24/11/2011;
accepted 19/9/2012)

دراسات علي الحلقات غير المتجانسة : طرق جديدة لتشييد مشتقات البيرول ، البيريدين ، البيرازولوبيريدين، البيرانوكينولين ، البنزوكرومين ، الكرومينوكرومين والكومارين

فتحي محمد عبد العزيز الطويل ،عبد الغني علي العجمي وشيماء محفوظ الموجي
قسم الكيمياء – كلية العلوم – جامعة دمياط – دمياط الجديدة – مصر .

نظرا للأهمية البيولوجية و الطبية للمركبات الأروماتية غير متجانسة الحلقة كمبيدات حشرية ، مضادات للملاريا وغير ذلك فقد إتجهنا إلي تشييد مشتقات جديدة من هذه المركبات مثل البيرول، البيريدين ، البيرازولوبيريدين ، البيرانوكينولين والبنزوكرومين والكرومينوكرومين من تفاعل المركبات ذات الهيدروجين النشيط مثل:
4- نيتروزوبيرازول 4 ،4-أزيدوميثيل كربونيل بيرازولين 8 ، 3- أسيتيل -4- هيدروكسي كينولين 15، ثنائي هيدروكسي نفثالين أرقام 24 ، 27، 29 ، 34 ، 35 و كذلك الثيازولين 39 مع النيتريلات أرقام 1 و2 غير المشبعة .

وقد تم إثبات التركيب البنائي للمركبات الجديدة بإستخدام الطرق الكيميائية و التحليل الطيفي مثل الأشعة تحت الحمراء والرنين النووي المغناطيسي.