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Studies with functionally substituted heteroaromatics: a new routes for synthesis of pyridazino[2,3-a] quinazoline and pyridazino-6-imine derivatives

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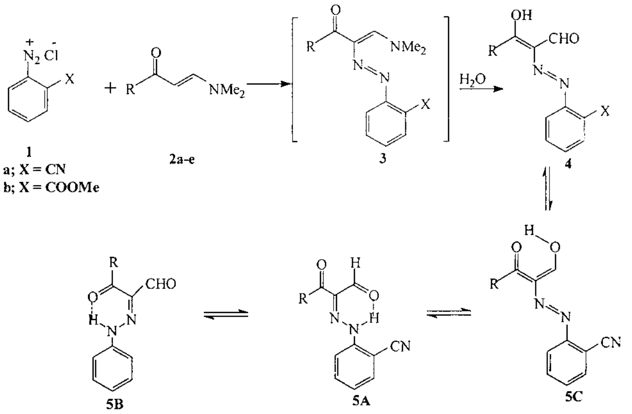
Enaminones couple with diazotized anthranilic acid derivatives yielding 2-arylhydra-zonopropanals that condensed with active methylenes yielding condensed pyridazines.

Recently,[10] aryldiazonium salts were successfully coupled with 3-N,N-dimethyl-aminol-oxo-2-propenes yielding 2-arylhydrazonopropanals. Likewise, it was found that diazotized anthranilonitrile **1a** couples readily with the enaminones **2a–e** to yield products of coupling and hydrolysis of dimethylamino moiety. The coupling products can thus be formulated as the arylhydra-zonopropanals **5** or potential tautomeric enol azo forms **4, 5A–C** or a mixture of one or more of these forms.

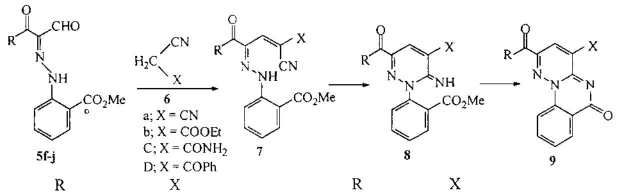
The aforementioned **5a–e** were produced by coupling at C-2′ of the α,β-unsaturated ketone with diazonium ion followed by hydrolysis of the substituent at 3-position into the formyl group by action of the aqueous base existing in the medium.

Similar to their behaviour towards diazotized anthranilonitrile **1a, 2a–e** coupled also with diazotized methyl anthranilate **1b** yielding a product of coupling and hydrolysis of the dimethylamine moiety. Again, the hydrazone structure **5f–j** was established for these products based on the appearance of the formyl proton at δ 10.23 in ^{1}H NMR and the hydrazone hydrogen proton at δ 15.66 ppm.

When diazotized anthranilonitrile **1a** was coupled with **2f**, a product of coupling and dimethylamine hydrolysis was also obtained. ^{1}H NMR of this product show that it exists in DMSO as an equilibrium mixture of *E*-form **5A**, *Z*-form **5B** and the enol azo form **5C**, as ^{1}H NMR revealed three signals for a total of one proton at δ 9.0, 9.6 and 10.2 ppm. The signal at δ 9.00 ppm is assigned for CH in the hydroxymethyl form while the signal at δ 9.6 ppm is assigned for the formyl proton in the *Z*-form and the one at δ 10.2 ppm is assigned for the formyl proton in the *E*-form.



	R	X		R	X
a	phenyl	CN	f	phenyl	CO_2Me
b	2-thienyl	CN	g	2-thienyl	CO_2Me
c	2-furyl	CN	h	2-furyl	CO_2Me
d	2-pyrrolyl	CN	i	2-pyrrolyl	CO_2Me
e	2-pyridyl	CN	j	2-pyridyl	CO_2Me
			k	CH_3	CN
			l	CH_3	CO_2Me

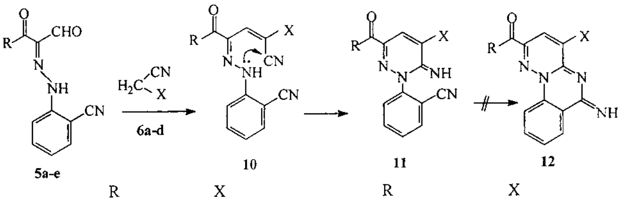


	R	X		R	X
a	phenyl	CN	h	2-thienyl	$CONH_2$
b	2-thienyl	CN	i	2-furyl	$CONH_2$
c	2-pyridyl	CN	j	phenyl	COPh
d	phenyl	CO_2Et	k	2-furyl	COPh
e	2-thienyl	CO_2Et	l	2-pyrrolyl	COPh
f	2-pyridyl	CO_2Et	m	CH_3	CN
g	phenyl	$CONH_2$	n	CH_3	COPh

From integrals, it could be calculated that the major constituent in this equilibrium mixture (70%) is the *E*-form, while (20%) of the *Z*-form also exist and the remaining (10%) exist in the enol azo form. All these forms are stabilized by hydrogen bonding.

The so obtained arylhydrazones have been utilized as starting materials for preparing the targeted condensed pyridazinone ring system. Thus, the arylhydrazones **5f,g,j** condensed readily and smoothly with the malononitrile **6a** in presence of a base in refluxing ethanol or dioxane yielding products of water and methanol elimination which can thus be formulated as the pyridazino[2,3-a]quinolinones **9a–c**. The formation of **9** from **5** and **6a** is assumed to proceed via intermediary of nonisolable **7** and **8**. Similarly, condensation of arylhydrazones **5f,g,j** with ethyl cyanoacetate **6b** afforded the pyridazinoquinazolines **9d–f**, while condensing the arylhydrazones **5f–i** with either cyanoacetamide **6c** or benzoylacetonitrile **6d** afforded the pyridazino[2,3-a]quinazolines **9g–l**.

Similarly, hydrazone **5l** condensed with malononitrile **6a** and benzoyl acetonitrile **6d** yielded the tricyclic pyridazino[2,3-a]quinazolines.



	R	X		R	X
a	phenyl	CN	h	phenyl	$CONH_2$
b	2-thienyl	CN	i	2-thienyl	$CONH_2$
c	2-furyl	CN	j	2-pyridyl	$CONH_2$
d	phenyl	CO_2Et	k	phenyl	COPh
e	2-thienyl	CO_2Et	l	2-thienyl	$CONH_2$
f	2-furyl	CO_2Et	m	2-pyridyl	$CONH_2$
g	2-pyridyl	CO_2Et			

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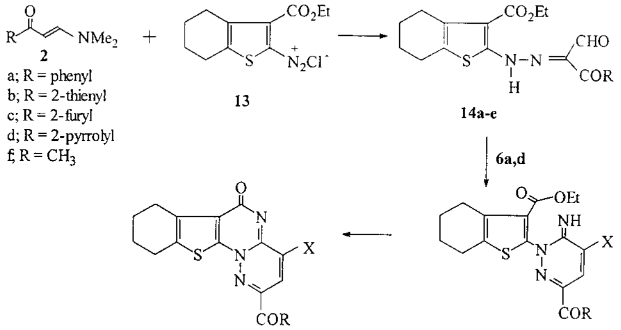
* To receive any correspondence.



16a-f **15**

	R	X		R	X
a	phenyl	CN	d	2-pyrrolyl	CN
b	2-thienyl	CN	e	CH_3	CN
c	2-furyl	CN	f	CH_3	COPh

Also, arylhydrazones **5a–e** condensed with malonoitrile **6a** yielding products of condensation and water elimination. These can be formulated as the arylhydrazone **10**, pyridazin-6-imine **11**, or pyridazino[2,3-a]quinazolines **12**.

Similar to their behaviour towards **6a**, compounds **5a–e** condensed also with **6b–d** yielding the pyridazin-6-imines **11d–m**, whose UV indicated that the targeted pyridazino[2,3-a]quinazoline ring was not formed.

The diazotized 2-aminocyclohexenethiophene[14] **13** coupled readily with **2a–d,f** to yield **14a–e**. Those compounds condensed with malononitrile **6a** to yield **16a–f** most likely via intermediacy of **15**.

Similarly, compound **13** coupled with **2f** yielding the hydrazone **14e** which condensed with **6a,d** yielding **16e** and **16f**.

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