Studies on the Synthesis and Cyclization Reactions of 2-(5-Amino-3-arylpyrazol-1-yl)-3-methylquinoxalines

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A series of 2-(5-amino-3-arylpyrazol-1-yl)-3-methylquinoxalines (**2a–d**) has been synthesized by the condensation of 2-hydrazino-3-methylquinoxaline (**1**) with substituted benzoylacetonitriles and converted into the corresponding 3,4-diaryl-1-(3-methylquinoxalin-2-yl)-4,8-dihydro-1*H*-pyrazolo[3,4-*e*][1,4]thiazepin-7(6*H*)-ones (**7a–d**) and 2-(3-aryl-4,5,6,7-tetrahydro-5-alkyl/aryl-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)-3-methylquinoxalines (**8a–e**).

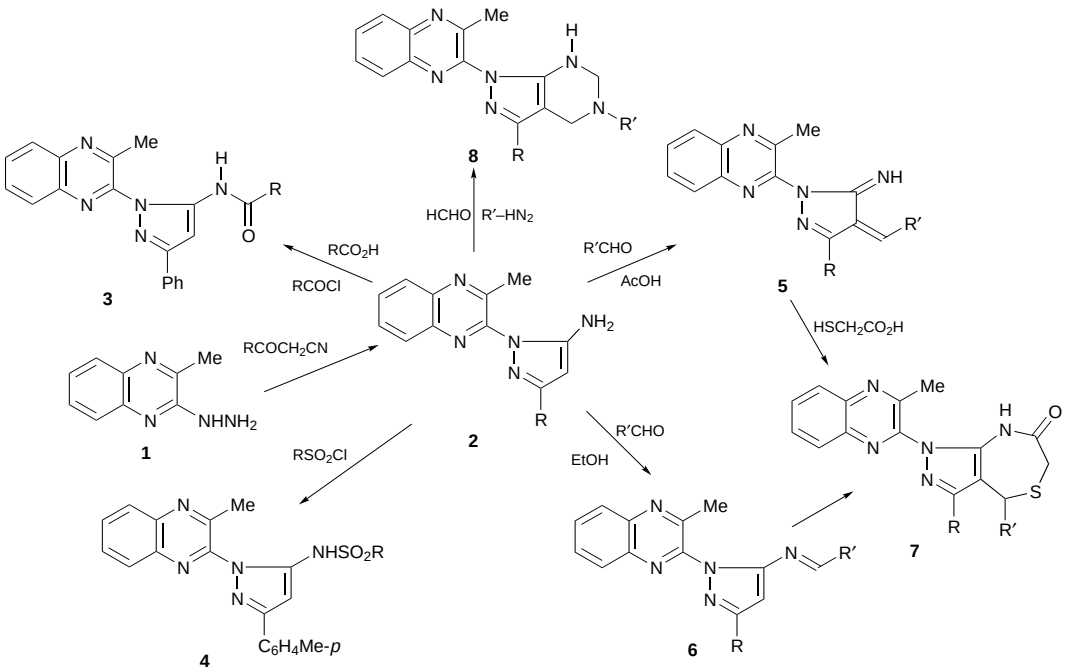
Quinoxaline derivatives have been found to be biologically active compounds having antibacterial, antifungal, anticancer, antiinflammatory, antidepressant, anthelmintic and herbicidal properties.[1–3] Likewise, pyrazole derivatives are reported to have antibacterial, antifungal and other biological activity.[4–7] In view of the above interest in these compounds and in continuation of our studies on the cyclization of hydrazino heterocyclic compounds we have investigated 2-hydrazino-3-methylquinoxaline in ring-closure reactions with substituted benzoylacetonitrile under different reaction conditions.

Condensation of 2-hydrazino-3-methylquinoxaline (**1**) with substituted benzoylacetonitriles either in boiling ethanol or by fusion led to the formation of 2-(5-amino-3-arylpyrazol-1-yl)-3-methylquinoxalines (**2**) (Scheme).

Condensation of the 3-phenylpyrazolyl derivative **2a** with formic, acetic or propionic acid afforded the corresponding *N*-acyl derivatives **3a–c**. Compounds **3b**,**d**,**e** were also obtained on treatment of **2a** with acetyl, chloroacetyl and benzoyl chloride[11] respectively. Refluxing of the *p*-tolyl derivative **2d** with arenesulfonyl chlorides[12] in chloroform containing anhydrous K_2CO_3 provided the corresponding *N*-arylsulfonyl derivatives **4a**,**b**. Condensation of **2** with aromatic aldehydes either in acetic acid or in toluene gave 2-(4-arylmethylidene-5-imino-3-arylpyrazol-1-yl)-3-methylquinoxalines (**5a–d**), while in ethanol containing a few drops of piperidine, as a catalyst, the corresponding Schiff's bases (**6a–d**) were the sole isolable products.[15]

Condensation of **5** with sulfanylacetic acid in boiling toluene gave 3,4-diaryl-1-(3-methylquinoxalin-2-yl)-4,8-dihydro-1*H*-pyrazolo[3,4-*e*][1,4]thiazepin-7(6*H*)-ones (**7a–d**). Interestingly, condensation of **6** with sulfanylacetic acid under the same reaction condition gave the same products **7**.

We also investigated the behaviour of **2** as a bifunctional nucleophile with formaldehyde and appropriate amines in order to study the reactivity at the 4- and 5-positions of the pyrazole moiety. When **2a**,**b** were treated with formaldehyde and primary amines in boiling ethanol only one pure product



2	R
a	Ph
b	C_6H_4Br-*p*
c	C_6H_4Cl-*p*
d	C_6H_4Me-*p*

3	R
a	H
b	Me
c	Et
d	CH_2Cl
e	Ph

4	R
a	Ph
b	C_6H_4Me-*p*

5-7	R	R′
a	Ph	C_6H_4Cl-*p*
b	C_6H_4Br-*p*	Ph
c	C_6H_4Cl-*p*	C_6H_4OMe-*p*
d	C_6H_4Me-*p*	C_6H_4Cl-*p*

8	R	R′
a	Ph	Me
b	Ph	Ph
c	Ph	C_6H_4Me-*p*
d	C_6H_4Br-*p*	Ph
e	C_6H_4Br-*p*	$C_6H_4NO_2$-*p*

Scheme

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8 was obtained. This could be formed *via* a double Mannich reaction.[17]

Techniques used: Elemental analysis, IR, ^{1}H NMR, mass spectrometry, TLC

References: 17

Schemes: 3

Tables: 3 (Yields, mps, spectral and analytical data for **2–8**)

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References cited in this synopsis

1 Y. Kurasawa and A. Takad, *Heterocycles*, 1986, **24**, 2321.
2 Y. Kurasawa, M. Muramatsu, K. Yamazaki, S. Tajima, Y. Okamoto and A. Takada, *J. Heterocycl. Chem*., 1986, **23**, 1379, 1391.
3 G. Skata, K. Makino and Y. Kurasawa, *Heterocycles*, 1988, **27**, 2481.
4 G. Vertuani, P. Giori, M. Guarneri and G. P. Sarto, *J. Pharm. Sci*., 1985, **74**, 1013.
5 P. Giori, T. Poli, C. B. Vicentini, M. Manfrini, M. Guarneri and V. Brandolini, *Farmaco, Ed. Sci*., 1985, **40**, 795.
6 C. B. Vincentini, T. Poli, M. Manfrini, M. Guarnerim, P. Giori and V. Brandolini, *Farmaco, Ed. Sci*., 1987, **42**, 133.
7 C. B. Vicentini, T. Poli, A. C. Veronese, V. Brandolini, M. Manfrini, M. Guarneri and P. Giori, *Pestic. Sci*., 1989, **27**, 77.
11 C. B. Vicentini, A. C. Veronese, P. Giori, B. Lumachi and M. Guarneri, *Tetrahedron*, 1990, **46**, 5777.
12 G. Szilagyi and P. Dvortsak, *Monatsh. Chem*., 1989, **120**, 131.
15 L. Jennig, J. Hofmann, M. Alva-Astudillo and G. Mann, *J. Prakt. Chem*., 1990,l **332**, 351.
17 M. Tramontini and L. Angiolini, *Tetrahedron*, 1990, **46**, 1791.