A FACILE SYNTHESIS OF CHROMONYL & QUINOLINYL 1,2,4-*s*-TRIAZOLO [4,3-a] QUINOXALINES BY DEHYDROGENATIVE CYCLIZATION USING DDQ.

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Abstract:

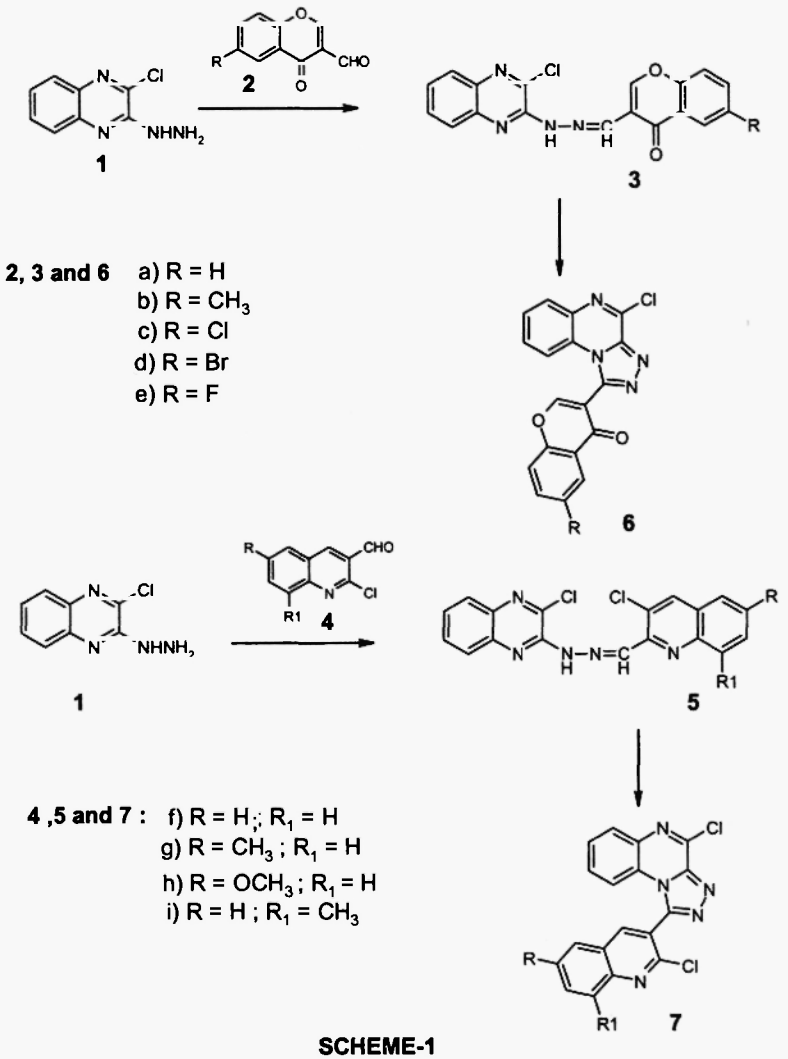
A series of chromonyl and quinolinyl 1.2.4-s-triazolo(4,3-a) quinoxalines (**6 and 7**) have been prepared by dehydrogenative cyclization of schiff's bases (**3 and 5**) derived from 2-chloro-3-hydrazinoquinoxlines (**1**) and 3-formylchromone (**2**) and 2-chloro-3-formylquinolines (4) using DDQ.

Introduction:

Several chromones are associated with important physiological properties such as antibacterial, antifungal[1] and diuretic activities[2]. Also a number of quinoline derivatives[3] have been reported to possess diverse types of biological properties. In addition, different triazoloquinoxalines[4-6] exhibited pharmacological activities such as antiallergic and antiinflammatory activities. Recently several amino 1,2,4-s-triazoloquinoxalines have been reported to display potent adrenosine receptor antagonist effects and have therapeutic potential as novel and rapid acting antidepressant agents[7]. In view of this, and in continuation of our work on the synthesis of new heterocyclic compounds derived from 3-formylchromones and 2-chloro-3-formylquinolines, we have synthesized a series of new chromonyl and quinolinyl substituted triazoloquinoxalines (**6 and 7**) (Scheme 1). In the present work, the title compounds were prepared by dehydrogenative cyclization of schiff's bases in the presence of DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone.)

Results and discussion:

The starting 2-Chloro-3-hydrazinoquinoxaline **1** was conveniently prepared by refluxing 2,3-dichloroquinoxaline[8] with hydrazinehydrate in methanol. The reaction of **1** with substituted 3-formyl chromones[9] (**2**) in chloroform at room temperature gave the corresponding schiff's bases **3** as crystalline products. Similarly the reaction of 1 with substituted 2-chloro 3-formylquinolines[10] in dimethyl formamide at room temperature gave the schiff's bases **5** in good yields (see Table 1). The arylidenes **3** & **5** have been characterized by NMR and other analytical data. **(3 and 5)** exhibited characterstic –CH=N in NMR.



SCHEME-1

Different methods have been reported for the cyclization of schiff's bases derived from hydrazinoquinoxalines and araldehydes, such as refluxing hydrazinoquinoxalines in presence of chloranil[11], cupric acetate in acetic acid[12] and bromine in acetic acid[5]. In the present work the chromonyl and quinolinyl triazolo quinoxalines (**6 and 7**) (see Table 1) were prepared in excellent yields by dehydrogenative cyclization of hydrazinoquinoxlines in presence of DDQ. Thus refluxing (**3 and 5**) in toluene in presence of DDQ gave the new triazoloquinoxalines as crystalline products. The structures of products have been characterized by analytical data supported by NMR[14].

Thus the present method offers a mild and rapid procedure for cyclization of hydrazinoquinoxalines.

Table 1: Percent yields of chemical transformation shown in scheme 1

Cmpd	R	R_1	3[a]	6[a]	5[a]	7[a]
a	H	-	83	92	-	-
b	CH_3	-	82	80	-	-
c	Cl	-	84	92	-	-
d	Br	-	87	83	-	-
e	F	-	98	96	-	-
f	H	H	-	-	86	81
g	CH_3	H	-	-	75	78
h	OCH_3	H	-	-	80	80
i	H	CH_3	-	-	97	80

(a) for melting points see reference **13**

Experimental:

General procedure for the preparation of **3**

A mixture of 2-chloro-3-hydrazinoquinoxaline **(1)** (0.154 mole) and 3-formylchromone **(2)** (0.154 mole) in chloroform (50 ml) was stirred at room temperature for 3 hrs. The separated solid was filtered, washed with chloroform and dried to give the product **(3)**.

General procedure for the preparation of **5**

A mixture of **(1)** (0.154 mole) and 2-chloro–3-formylquinoline **(4)** (0.154 mole) in dimethylformamide (30 ml) was stirred at room temperature for 3 hrs. The separated solid was filtered, washed with methanol and dried to give the product **5**.
The analytical and spectral data of schiff's bases were presented in Table -1.

General procedure for the preparation of **6 and 7**

A mixture of schiff's base **(3** or **5)** (0.0025 mole) and dichlorodicyanol,4-benzoquinone DDQ (0.0025 mole) in toluene (15 ml) was refluxed for 1 hr. The reaction was monitored by TLC and after completion of the reaction, it was filtered, washed with methanol and dried to give pure **(6 and 7)**.

1-(2-chloro-6-methylquinolin-3-yl)-1,2,4-s-triazolo-(4,3-a) quinoxaline:7h(R=OCH_3)

The arylidene derivative ***5h*** was converted to ***7h*** (R = -OCH_3) according to the general procedure for the preparation of 7 to give 7*h* (80%) as crystalline solid. Melting point >300 ^{0}C H^1 NMR (200 MHz, DMSO-d6): δ 3.99 (s, 3H, OCH3) 7.20-7.7.0 (m, 5H, ArH) 8.00-8.20 (m, 2H, ArH) 8.6 (s,1H, ArH).

Anal. Calcd. for C_{19} $H_{11}Cl_2N_5O$: C,57.57;H,2.77;N,17.6.found: C, 57.87; H, 3.01;N,17.7.

The analytical and spectral data of triazoloquinoxalines 6 and 7 have been presented in references 13 and 14.

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13. Melting points of crystalline products: **3a**, 208^0; **3b**, 205^0; **3c**, 208; **3d**, 210^0; **3e**, 218; **5f**, 219^0; **5g**, 222^0; **5h**, 221^0, **5i**, 224^0, **6a**, >300^0, **6b**, >300^0; **6c**, >300^0; **6d**, >300^0; **6e**, >300^0; **7f**, >300^0; **7g**, >300^0; **7h**, >300^0; **7i**, >300^0.
14. Representative ^{1}H NMR spectra: **3a**, (DMSO): δ 7.45-7.90 (m, 7H, ArH), 8.20 (d, 1H, J=7.8 Hz, ArH), 8.80 (s, 1H,-CH=N), 8.90 (s, 1H, ArH), 11.2 (bs, 1H, NH). **3b**, (DMSO): δ 2.5 (s, 3H,-CH3), 7.50-8.00 (m, 7H, ArH); 8.80 (s, 1H; ~CH=N), 8.85 (s, 1H, ArH), 11. 10 (bs, 1H, NH). **3c** (DMSO): δ 7.40-8.10 (M, 7H, ArH), 8.80 (s, 1H, CH=N); 8.90 (s, 1H, ArH), 11.30 (bs, 1H, NH). **3d** (DMSO): δ 7.40-7.90(m, 7H, ArH), 8.25 (s, 1H,-CH=N) 8.80 (S, 1H, ArH), 11.00 (bs, 1H, NH). **3e** (DMSO): δ 7.40-7.90(m, 7H, ArH), 8.70 (s, 1H,-CH=N) 8.90 (s, 1H, ArH), 11.20 (bs, 1H, NH). **5f** (DMSO): δ 7.40-8.10(m, 8H, ArH), 9.00 (s, 1H,-CH=N); 9.10 (S, 1H, ArH), 9.40 (bs, 1H, NH). **5g** (CD Cl_3); δ 2.50-(s, 3H, -CH_3), 7.40-8.10(m, 7H, ArH); 8.80 (s, 1H,-CH=N), 9.00 (s, 1H, ArH), 9.35 (bs, 1H, NH). **5h** ($CDCl_3$): δ 4.00 (s, 3H, -OCH_3), 7.10-8.10(m, 6H, ArH), 8.70 (s, 1H, ArH) 9.00 (s, 1H, ArH), 9.30 (s, 1H, CH=N) 9.80 (bs, 1H, NH). **5i** ($CDCl_3$): δ 2.70 (s, 3H, CH_3), 7.20-8.10 (m, 7H, ArH), 8.75 (s, 1H, -CH=N), 9.00 (s, 1H, ArH), 9.20 (bs, 1H, NH). **6a** (DMSO): δ 7.50-7.95(m, 6H, ArH), 8.05 (d, 1H, J=7.9HZ, ArH) 8.25 (d, 1H, J=7.9HZ, ArH). **6b** (DMSO): δ 2.50 (s, 3H, CH_3), 7.50-8.15 (m, 7H, ArH), 8.85 (s,, 1H, ArH). **6c** (DMSO): δ 7.60-8.30 (m, 7H, ArH), 9.05 (s, 1H, ArH). **6d** (DMSO): δ 7.60-8.20 (m, 7H, ArH); 9.00 (s, 1H, ArH). **6e** (DMSO): δ 7.60-8.10 (m, 7H, ArH), 9.00 (s, 1H, ArH). **7f** (DMSO): δ 7.20-8.30 (m, 7H, ArH), 8.55 (s, 1H, ArH) 9.00 (s, 1H, ArH). **7g** (DMSO): δ 2.60 (s, 3H, CH_3) 7.20-8.20 (m, 7H, ArH); δ.80 (s, 1H, ArH). **7i** (DMSO): δ 2.80 (s, 3H, -CH_3); 7.20-8.20 (m, 7H, ArH); 9.00 (s, 1H, ArH).

Received on January 20, 2003