

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:

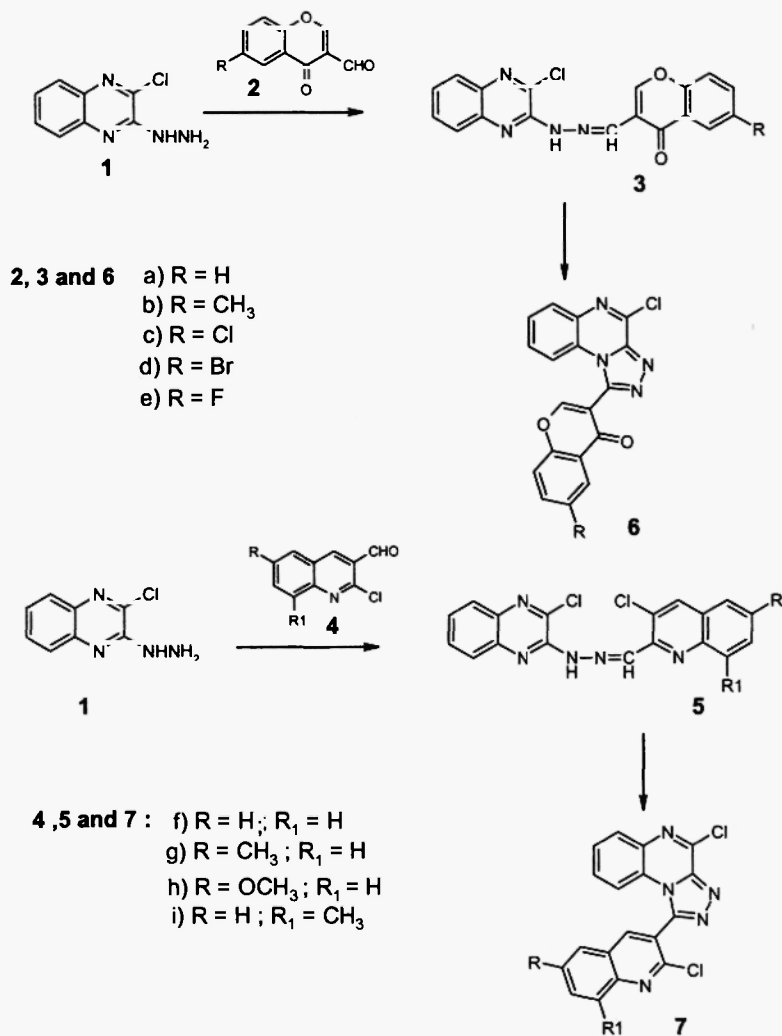
A series of chromonyl and quinolinyll 1.2.4-s-triazolo(4,3-a) quinoxalines (**6 and 7**) have been prepared by dehydrogenative cyclization of schiff's bases (**3 and 5**) derived from 2-chloro-3-hydrazinoquinoxalines (**1**) and 3-formylchromone (**2**) and 2-chloro-3-formylquinolines (**4**) using DDQ.

Introduction:

Several chromones are associated with important physiological properties such as antibacterial, antifungal¹ and diuretic activities². Also a number of quinoline derivatives³ have been reported to possess diverse types of biological properties. In addition, different triazoloquinoxalines⁴⁻⁶ exhibited pharmacological activities such as antiallergic and antiinflammatory activities. Recently several amino 1,2,4-s-triazoloquinoxalines have been reported to display potent adenosine receptor antagonist effects and have therapeutic potential as novel and rapid acting antidepressant agents⁷. 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 quinolinyll 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-dichloroquinoxaline⁸ with hydrazinehydrate in methanol. The reaction of **1** with substituted 3-formyl chromones⁹ (**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-formylquinolines¹⁰ 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 characteristic --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 chloranil¹¹, cupric acetate in acetic acid¹² and bromine in acetic acid⁵. 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 hydrazinoquinoxalines 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 NMR¹⁴.

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 dichlorodicyanil,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=OCH₃)

The arylidene derivative **5h** was converted to **7h** (R = -OCH₃) according to the general procedure for the preparation of **7** to give **7h** (80%) as crystalline solid. Melting point >300 °C ¹H 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 C₁₉ H₁₁Cl₂N₅O: 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**, 208⁰; **3b**, 205⁰; **3c**, 208; **3d**, 210⁰; **3e**, 218; **5f**, 219⁰; **5g**, 222⁰; **5h**, 221⁰, **5i**, 224⁰, **6a**, >300⁰, **6b**, >300⁰; **6c**, >300⁰; **6d**, >300⁰; **6e**, >300⁰; **7f**, >300⁰; **7g**, >300⁰; **7h**, >300⁰; **7i**, >300⁰.
14. Representative ¹H 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** (CDCl₃): δ 2.50-(s, 3H, -CH₃), 7.40-8.10(m, 7H, ArH); 8.80 (s, 1H, -CH=N), 9.00 (s, 1H, ArH), 9.35 (bs, 1H, NH). **5h** (CDCl₃): δ 4.00 (s, 3H, -OCH₃), 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** (CDCl₃): δ 2.70 (s, 3H, CH₃), 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, CH₃), 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, CH₃) 7.20-8.20 (m, 7H, ArH); δ.80 (s, 1H, ArH). **7i** (DMSO): δ 2.80 (s, 3H, -CH₃); 7.20-8.20 (m, 7H, ArH); 9.00 (s, 1H, ArH).

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