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Note

Synthesis of some 4-substituted hydrazinotetrazolo[1,5-*a*]quinoxalines

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Reaction of 2,3 diketoquinoxaline in presence of phosphorus pentachloride and sodium azide in methanol gives 4-hydroxy tetrazolo[1,5-*a*]quinoxaline **3** which on reaction with phosphorous oxychloride gives 4-chloro tetrazolo[1,5-*a*]quinoxaline **4.** This on treatment with hydrazine hydrate in ethanol yields 4-hydrazino tetrazolo[1,5-*a*]quinoxaline **5**, which on reaction with various aldehydes in DMF gives 4-substituted hydrazinotetrazolo [1,5-*a*]quinoxalines **6a-g**. The structures of compounds **6a-g** have been confirmed by IR and ^{1}H NMR.

Keywords: Quinoxaline, NMDA receptor, biological activity

Quinoxaline derivatives are very useful compounds with well-known biological activity[1,2]. Whereas quinoxaline compounds are important components of several pharmacologically active moieties[3]. Certain quinoxaline 2,3-diones and quinoxaline 2-ones were highly potent NMDA receptor antagonists. Hence, due to this commendable biological activity the synthesis of some new 4-substituted hydrazine tetrazolo[1,5-*a*]quinoxalines was reported. Also quinoxaline based materials were used as ETLs or (Electron transporting layer) or hole blocking layers in OLEDs (organic light emitting diodes)[4,5].

Results and Discussion

2,3-Diketoquinoxaline **1** by reacting with phosphorus pentachloride and sodium azide to form compound **3**. The disappearance of (C=O) peak at 1720 cm^{-1} and appearance of broad peak at 3300-3400 cm^{-1} due to –OH confirm the formation of compound **3**. The compound **3** on reaction with phosphorous oxychloride followed by hydrazine hydrate in methanol yield the compound **5**. The compound **5** shows sharp peak at 3286 and 3190 cm^{-1} due to NH and NH_2. The ^{1}H NMR spectrum of compound **2** shows a broad signal at δ 4.20 due to NH_2 protons and at δ 6.6 the characteristics of NH proton. The compound **5** on reaction with various aldehydes form compound **6a-g** (**Scheme I**). The disappearance of 3286 and 3190 cm^{-1} peaks and appearance of band at 3299 cm^{-1} due to –NH stretching confirm the formation of compound **6**. The 4-substituted hydrazinotetrazolo[1,5-*a*]quinoxalines show disappearance of NH_2 proton signal while that of NH signal are shifted at δ 10-12.5 as a result of deshielding effect of HC=N- group in all compounds. The proton of azomethine (-N=CH-) group leads to a sharp singlet at δ 8.5- 9.5 in all compounds (**Table I**).

Experimental Section

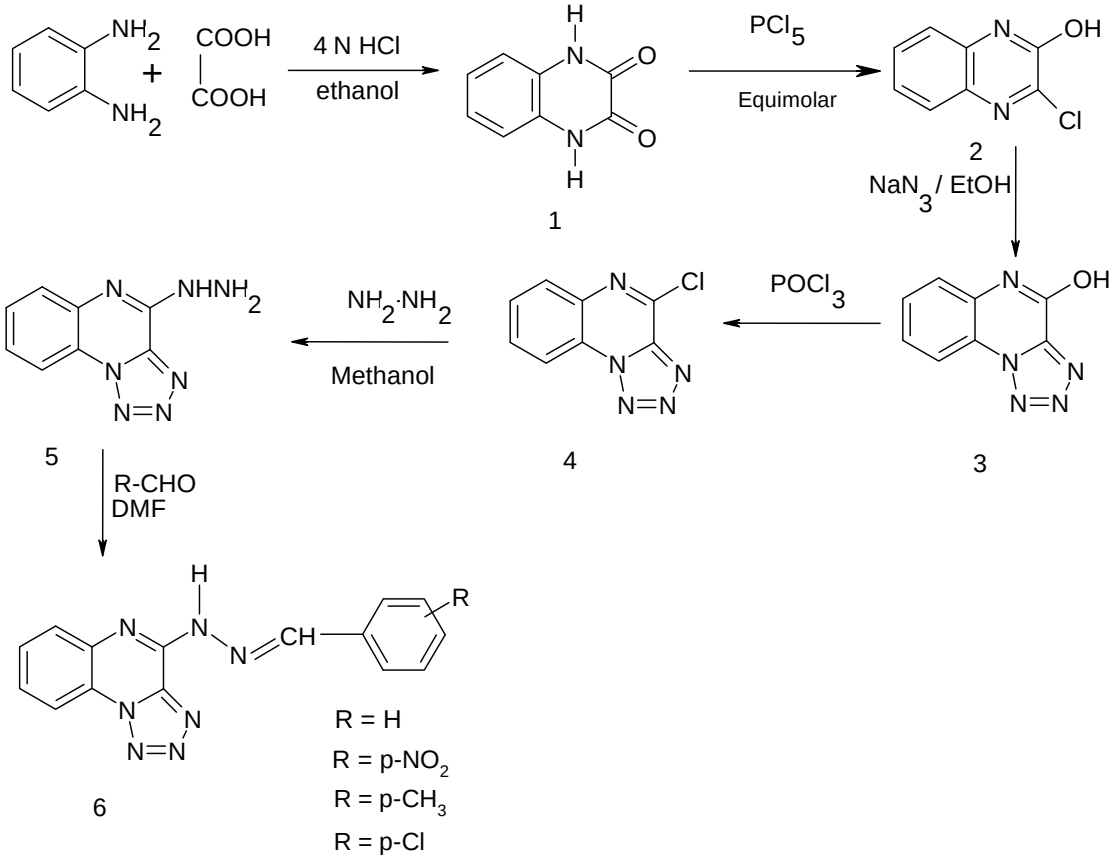
All melting points are determined in an open capillary tube and are found to be uncorrected. Infrared spectra were measured on a Perkin-Elmer-783 spectrophotometer. ^{1}H NMR data were recorded on 300 MHz spectrophotometer using $CDCl_3$ and DMSO-d_6 as a solvent with TMS as an internal standard. All reagents were of commercial quality (Aldrich, Lancaster, Fluka, and Merk). Reactions were monitored by thin layer chromatography (TLC) on glass plates. Column chromatography was carried out on silica gel.

2,3-Diketoquinoxaline 1. *o*-Phenylene diamine (27.9 g, 0.25 mole), oxalic acid (32.5 g, 0.36 mole) and 4 *N* HCl (150 mL) were refluxed on oil-bath for 1 and half hr, and cooled. The solid separated was filtered and washed. m.p. < 300°C. Yield 85%; colourless needle shaped crystals. IR (KBr) 3350, 2928, 28, 1658, 1593, 1028 cm^{-1}.

4-Chloro tetrazolo[1,5-*a*]quinoxaline 4. The homogeneous mixture of compound **1** (2 g, 0.10 mole) and phosphorous pentachloride (2 g, 0.10 mole) was refluxed on oil-bath for 6 hr. The reaction mixture was cooled and poured on crushed ice to get yellowish product, which was filtered and recrystallised with rectified spirit, m.p. 154°C. The compound **2** (1 g, 0.20 mole) and sodium azide (1 g, 0.20 mole) was refluxed for 2 hr on oil bath and with routine laboratory work-up the 4-hydroxy tetrazolo[1,5-*a*]quinoxaline **3** was obtained which further reacted with phosphorous oxychloride (equimolar quantity) to get 4-chloro tetrazolo[1,5-*a*]quinoxaline **4**, m.p. 264°C; IR (KBr) 3264, 3054, 2836, 1591, 1496 cm^{-1}.

Table I — NMR spectral data of compounds **6a-g**

No	R	X	NH	CH	Ar-H
6a	C_6H_4	-	11.1 (s, 1H)	8.70 (s, 1H)	8.3-7.10 (m, 9H)
6b	$3NO_2C_6H_4$	-	11.3 (s, 1H)	8.82 (s, 1H)	8.6-7.20 (m, 8H)
6c	4- $CH_3C_6H_4$	2.30 (s, 3H)	11.0 (s, 1H)	9.65 (s, 1H)	8.2-7.20 (m, 8H)
6d	4-$OMeC_6H_4$	3.85 (s, 6H)	11.0 (s, 1H)	8.92 (s, 1H)	8.3-7.40 (m, 8H)
6e	4-Cl-C_6H_4	-	11.9 (s, 1H)	8.70 (s, 1H)	8.3-7.22 (m, 8H)
6f	$[(4N,N,(CH_3)_2]C_6H_4$	3.83 (s, 6H)	12.0 (s, 1H)	8.33 (s, 1H)	8.3-7.24 (m, 8H)
6g	$[(3,4,5(OCH_3)_3]C_6H_2$	3.87 (s, 9H)	9.87 (s, 9H)	8.59 (s, 1H)	6.7-7.65 (m, 6H)



Scheme I

4-Hydrazine tetrazolo[1,5-*a*]quinoxaline 5. The compound **4** (0.500 g 0.001 mole) on heating with hydrazine hydrate (1.5 mL) in methanol on water for 2 hr yielded yellowish white coloured product, m.p. 187°C IR (KBr) 3106, 2936, 2845, 1592, 1490, 1388 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 4.20 (s, 2H, NH_2), 6.6 (s, 1H, NH), 7.04-7.56 (m, 4H, Ar-H).

4-Substituted hydrazine tetrazolo[1,5-*a*]quinoxalines 6. The compound **5** (1:1 mole) on refluxing with DMF with various aromatic aldehydes for 2-3 hr afforded the solid products in good yields.

4-(Benzylidenehydrazino) tetrazolo[1,5-*a*]quinoxaline 6a. Yield 83%, m.p. 308°C; IR (KBr) 3260, 1635, 760 cm^{-1}. ^1H NMR (300 MHz DMSO-d_6): δ 11.15 (s, 1H, NH), 8.70 (s, 1H, CH), 8.30-7.10 (m, 9H, Ar-H) Anal. Calcd for $C_{15}H_{11}N_7$: C, 64.07; H, 6.87; N, 29.07. Found: C, 63.01; H, 7.02; N, 28.09%.

4-(*m*-Nitrobenzylidene) hydrazinotetrazolo[1,5-*a*]quinoxaline 6b Yield 60%, m.p. 234°C; IR (KBr) 3326, 1640, 1525, 1350 cm^{-1}, ^1H NMR (300 MHz DMSO-d_6): δ 11.38 (s, 1H, NH), 8.82 (s, 1H, CH), 8.60-7.20 (m, 8H, Ar-H) Anal. Calcd for $C_{15}H_{10}N_8O_2$:

C, 56.53; H, 5.80; N, 29.30. Found: C, 55.09; H, 6.03; N, 28.54%.

4-(*p*-Methylbenzylidene) hydrazinotetrazolo[1,5-*a*]quinoxaline 6c.Yield 69%, m.p. 193°C; IR (KBr) 3330, 1640, 1480, 1330 cm^{-1}, ^1H NMR (300 MHz DMSO-d_6): δ 2.30 (s, 3H, CH_3), 11.11 (s, 1H, NH), 8.65 (s, 1H, CH), 8.28-7.20 (m, 8H, Ar-H); Anal. Calcd for $C_{16}H_{13}N_7$: C, 64.93; H, 7.17; N, 27.90. Found: C, 63.09; H, 7.09; N, 26.09%.

4-(*p*-Methoxybenzylidene)hydrazinotetrazolo-[1,5-*a*]quinoxaline 6d. Yield 75%, m.p. 218°C; IR (KBr) 3320, 1630, 1600, 1480, 1255 cm^{-1}, ^1H NMR (300 MHz DMSO-d_6): δ 3.85 (s, 3H, CH_3), 11.06 (s, 1H, NH), 8.62 (s, 1H, CH), 8.62-7.20 (m, 8H, Ar-H) Anal. Calcd for $C_{16}H_{13}N_7O$: C, 62.11; H, 6.86; N, 26.68. Found: C, 62.09; H, 6. 39; N, 25.09%.

4-(*p*-Chlorobenzylidene) hydrazinotetrazolo[1,5-*a*]quinoxaline 6e. Yield 63%, m.p. 230°C; IR (KBr) 3320, 1645, 1600, 1480, 1250 cm^{-1}, ^1H NMR (300 MHz DMSO-d_6): δ 11.09 (s, 1H, NH), 8.70 (s, 1H, CH), 8.30-7.22 (m, 8H, Ar-H) ppm Anal. Calcd for $C_{15}H_{11}N_7Cl$: C, 58.14; H, 5.96; N, 26.37. Found: C, 57.09; H, 5.29; N, 26.09%.

4-(N,N Dimethylbenzylidene) hydrazinotetrazolo [1,5-*a*] quinoxaline 6f. Yield 65%, m.p. 247°C; IR (KBr) 3048, 1681, 1607, 1472, 1391, 1247 cm^{-1}, ^1H NMR (300 MHz DMSO-d_6): δ 3.83 [s, 6H, $(CH_3)_2$], 12.1 (s, 1H, NH), 8.33 (s, 1H, CH), 8.30-7.24 (m, 8H, Ar-H) Anal. Calcd for $C_{17}H_{16}N_8$: C, 64.93; H, 7.17; N, 27.90. Found: C, 63.9; H, 6.09; N, 26.63%.

4-(3,4,5 Trimethoxybenzylidene) hydrazine-tetrazolo[1,5-*a*]quinoxaline 6g. Yield 70%, m.p. 287°C; IR (KBr) 3070, 2871, 2842, 1956, 1683, 1586, 1331, 1233 cm^{-1}, ^1H NMR (300 MHz DMSO-d_6): δ 3.87 [s, 9H, $(OCH_3)_3$], 9.87 (s, 1H, NH), 8.59 (s, 1H, CH), 7.67- 6.65 (m, 6H, Ar-H) Anal. Calcd for $C_{18}H_{17}N_7O_3$: C, 59.00; H, 6.84; N, 22.93. Found: C, 58.90; H, 6.09; N, 22.72%.

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