

Synthesis of quinoxalines catalysed by cetyltrimethyl ammonium bromide (CTAB) in aqueous media

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A facile and simple method has been developed for the condensation of 1,2-diaminobenzenes with α -bromoketones to form quinoxalines with good yields using cetyltrimethyl ammonium bromide (CTAB) in aqueous media. The efficiency of this reaction was demonstrated by the compatibility with nitro, methyl, methoxy, fluoro chloro bromo and furanyl groups. The important features of the methodology are broad substrate scope, simple workup, and no requirement for metal catalysts.

Keywords: quinoxaline, cetyltrimethyl ammonium bromide (CTAB), aqueous media

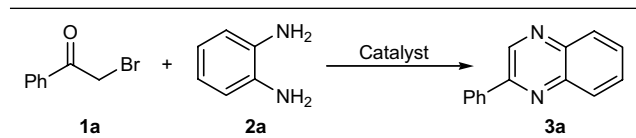
Quinoxaline derivatives have shown a broad spectrum of biological activities such as anticancer, anthelmintic, antifungal and insecticidal agents.¹ The quinoxaline ring is present in a number of antibiotics such as echinomycin, levomycin, and actinomycin, which are known to inhibit the growth of gram-positive bacteria and are also active against various transplantable tumours.^{2,3} They have also found applications as dyes,⁴ efficient electroluminescent materials,⁵ organic semiconductors,⁶ dehydroannulenes,⁷ cavitands⁸ and chemically controllable switches.⁹ Thus, a large number of procedures have been developed for the construction of quinoxaline derivatives involving condensation of 1,2-diamines with 1,2-diketones,^{10,11} oxidation-trapping of α -hydroxyketones with 1,2-diamines,^{12–14} 1,4-addition of 1,2-diamines to diazenylbutenes,¹⁵ POCl₃-mediated heteroannulation of α -nitroketene *N,S*-anilinoacetals,¹⁶ oxidative coupling of epoxides with ene-1,2-diamines,¹⁷ cyclisation–oxidation of phenacyl bromides and *o*-phenylenediamines through solid-phase synthesis^{18,19} or high temperature and pressure^{20,21} (150 °C and 20 psi) by microwave irradiation or using HClO₄·SiO₂²² as heterogeneous catalyst. Nevertheless, most of these methods suffer from drawbacks such as unsatisfactory yields, difficult experimental procedures, expensive and harmful reagents and harsh reaction conditions. Therefore, the development of environmentally benign, efficient and high-yielding methods for the synthesis of quinoxalines remains a highly desirable goal in organic synthesis.

In continuation of our efforts to develop green synthetic routes for the formation of C–C and carbon–heteroatom bond,^{23–32} we report here a green, simple and practical method for the synthesis of quinoxaline derivatives from α -bromoketones and 1,2-diaminobenzenes catalysed by CTAB in aqueous media.

At the onset of the research, the efficacy of various catalysts was investigated in the model reaction between α -bromoketone **1a** and 1,2-diaminobenzene **2a** under different reaction conditions (Table 1). The results showed that CTAB was superior with respect to product yields. Entry 1 shows the control reaction without addition of any catalyst, in this case 2-phenylquinoxaline **3a** was obtained in low yield. We next planned to determine the influence of solvent on the rate and yield of the model reaction. As shown in Table 1, the presence of organic solvents lowers the reaction rate (Table 1, entries 9–12). So we chose to perform this reaction in aqueous media. The structure of **3a** was characterised by ¹H NMR, ¹³C NMR, IR and by comparison with authentic samples prepared by a literature procedure.

With the optimised conditions in place, the reactions of various α -bromoketones with different 1,2-diaminobenzenes

Table 1 Synthesis of 2-phenylquinoxaline under different reaction conditions^a

			
Entry	Catalyst	Solvent	Yield/% ^b
1	none	H ₂ O	29
2	SDS	H ₂ O	52
3	TBAF	H ₂ O	50
4	TBAI	H ₂ O	51
5	TMAB	H ₂ O	64
6	CTAB	H ₂ O	81
7	CTAB	H ₂ O	53 ^c
8	CTAB	H ₂ O	70 ^d
9	CTAB	EtOH	60
10	CTAB	CH ₃ CN	59
11	CTAB	1,4-dioxane	61
12	CTAB	DMSO	70

^aAll the reactions were run with α -bromoketone **1a** (1.0 mmol), 1,2-diaminobenzene **2a** (1.2 mmol) and catalyst (25 mol%) in water (5 mL) at reflux for 8 h.

^bIsolated yield.

^c5 mol%.

^d10 mol%.

were examined to explore the scope and generality of this protocol for the synthesis of various quinoxalines and the results are summarised in Table 2.

As shown in Table 2, the substituent groups on the aromatic ring of the α -bromoketone had no obvious effect on the yields. It was observed that the α -bromoacetophenones with electron-donating functionality as well as electron-withdrawing functionality undergo condensation reactions with 1,2-diaminobenzenes equally well to afford the corresponding products in good to excellent yields. When employing the more hindered α -methylphenacyl bromide and 1,2-diaminobenzenes, moderate to good yields were also obtained (Table 2, entries 8, 17 and 22). Compared with the unsubstituted diamine, the reaction of most aromatic diamines bearing two substituents with α -bromoketones gave slightly lower product yields (Table 2, entries 11–22). The results showed that the scope of the reaction is quite broad and the conditions are tolerant of various functional groups such as nitro, methyl, methoxy, fluoro, chloro, bromo and furan groups.

In conclusion, we have developed an eco-friendly synthesis of quinoxalines catalysed by CTAB in water. Compared to previous reported methodologies, the present protocol features broad substrate scope, good yields, simple workup and has no requirement for metal catalysts. Further investigations on the

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Table 2 Synthesis of quinoxalines using CTAB in water^a

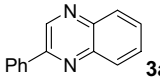
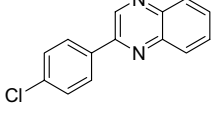
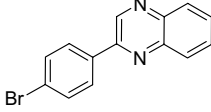
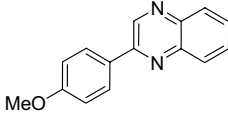
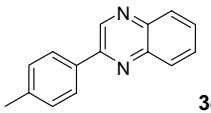
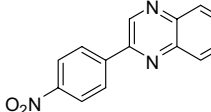
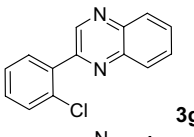
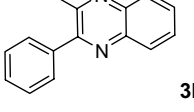
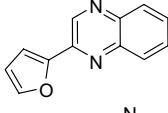
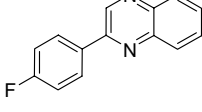
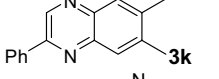
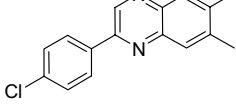
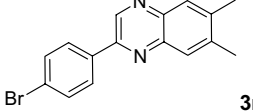
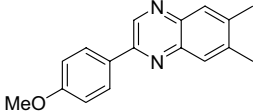
$ \begin{array}{c} \text{Ar} \quad \text{O} \\ \quad \quad \parallel \\ \text{---} \text{C} \text{---} \text{Br} \\ \quad \quad \\ \quad \quad \text{R}^1 \end{array} + \begin{array}{c} \text{H}_2\text{N} \quad \text{R}^2 \\ \quad \quad \quad \quad \\ \text{---} \text{C}_6\text{H}_3 \text{---} \\ \quad \quad \quad \quad \\ \text{H}_2\text{N} \quad \text{R}^2 \end{array} \xrightarrow[\text{water}]{\text{CTAB}} \begin{array}{c} \text{R}^1 \quad \text{N} \quad \text{R}^2 \\ \quad \diagdown \quad \diagup \\ \text{---} \text{C} \quad \text{C} \text{---} \\ \quad \diagup \quad \diagdown \\ \text{Ar} \quad \text{N} \quad \text{R}^2 \end{array} $					
Entry	α -Bromoketone		R ²	Products	Yield/% ^b
	Ar	R ¹			
1	C ₆ H ₅	H	H	 3a	81 ^c
2	<i>p</i> -ClC ₆ H ₄	H	H	 3b	92
3	<i>p</i> -BrC ₆ H ₄	H	H	 3c	95
4	<i>p</i> -MeOC ₆ H ₄	H	H	 3d	96 ^c
5	<i>p</i> -MeC ₆ H ₄	H	H	 3e	87 ^c
6	<i>p</i> -NO ₂ C ₆ H ₄	H	H	 3f	81
7	<i>o</i> -ClC ₆ H ₄	H	H	 3g	90
8	C ₆ H ₅	Me	H	 3h	71
9	2-furyl	H	H	 3i	80
10	<i>p</i> -FC ₆ H ₄	H	H	 3j	88
11	C ₆ H ₅	H	Me	 3k	89 ^c
12	<i>p</i> -ClC ₆ H ₄	H	Me	 3l	81
13	<i>p</i> -BrC ₆ H ₄	H	Me	 3m	85
14	<i>p</i> -MeOC ₆ H ₄	H	Me	 3n	80

Table 2 Continued

Entry	α -Bromoketone		R ²	Products	Yield/% ^b
	Ar	R ¹			
15	<i>p</i> -NO ₂ C ₆ H ₄	H	Me		71
16	<i>o</i> -ClC ₆ H ₄	H	Me		85
17	C ₆ H ₅	Me	Me		52
18	C ₆ H ₅	H	Cl		81
19	<i>p</i> -MeOC ₆ H ₄	H	Cl		75
20	<i>p</i> -NO ₂ C ₆ H ₄	H	Cl		70
21	<i>o</i> -ClC ₆ H ₄	H	Cl		60
22	C ₆ H ₅	Me	Cl		85

^aAll reactions were run with α -bromoketone **1** (1.0 mmol), 1,2-diaminobenzene **2** (1.2 mmol), CTAB (25 mol%, 0.25 mmol) and water (5 mL) at reflux for 24 h.

^bIsolated yield.

^cThe reaction was carried out for 8 h.

reaction mechanism, scope and limitations of these reactions and a biological evaluation of the new class of compounds are under way.

Experimental

Chemicals were purchased and used without further purification. Melting points were recorded on Digital Melting Point Apparatus WRS-1B and are uncorrected. IR spectra were recorded on a Bruker-EQUINOX55 spectrometer. Mass spectra (EI, 70 eV) were measured with SHIMADZU GCMS-QP2010 Plus instrument. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AC 300 instrument using CDCl₃ or DMSO-*d*₆ or acetone-*d*₆ as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts were given in δ relative to TMS, the coupling constants *J* are given in Hz. Elemental analysis was determined on a Carlo-Erba 1108 instrument. Column chromatography was performed using EM Silica gel 60 (300–400 mesh). All known products were identified by comparison with authentic samples.

General synthetic procedure for synthesis of 2-substituted quinoxalines of **3a–o**

To a mixture of α -bromoketone **1** (1 mmol) and 1,2-diaminobenzene **2** (1.2 mmol), CTAB (25 mol%) was added in water (5 mL) under reflux. The reaction was monitored by TLC. After completion of the reaction, the product was extracted with ethyl acetate (3 $\times$ 10 mL),

the organic layer washed with brine (3 $\times$ 10 mL), and then dried over anhydrous Na₂SO₄ and concentrated. The product was separated and purified by column chromatography on silica gel (300–400 mesh) using an ethyl acetate/petrol mixture as the eluent to afford a pure product. When necessary, the products are purified by recrystallising with an ethyl acetate/petrol mixture.

2-Phenylquinoxaline (3a): Solid, m.p. 74–76 °C (lit.³³ 75–76 °C); ¹H NMR (300 MHz, CDCl₃): δ 7.56–7.59 (m, 3H), 7.77–7.81 (m, 2H), 8.13–8.23 (m, 4H), 9.35 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 127.4, 127.7, 129.0, 129.3, 129.5, 130.0, 130.1, 136.5, 141.4, 142.1, 143.2, 151.5.

2-(4-Chlorophenyl)quinoxaline (3b): Solid, m.p. 12–128 °C (not reported);²² ¹H NMR (300 MHz, CDCl₃): δ 7.53–7.56 (m, 2H), 7.56–7.81 (m, 2H), 8.11–8.18 (m, 2H), 9.31 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 128.7, 129.1, 129.4, 129.6, 129.7, 130.4, 135.1, 136.6, 141.6, 142.2, 142.8, 150.5.

2-(4-Bromophenyl)quinoxaline (3c): Solid, m.p. 136–139 °C (not reported);¹³ ¹H NMR (300 MHz, CDCl₃): δ 7.63–7.66 (m, 2H), 7.74–7.76 (m, 2H), 8.02–8.11 (m, 2H), 9.24 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 124.91, 128.89, 129.09, 129.51, 129.73, 130.40, 132.25, 135.47, 141.57, 142.10, 142.70, 150.48.

2-(4-Methoxyphenyl)quinoxaline (3d): Solid, m.p. 100–101 °C (lit.³³ 99–100 °C); ¹H NMR (300 MHz, CDCl₃): δ 3.88 (s, 3H), 7.05–7.08 (m, 2H), 7.71–7.75 (m, 2H), 8.07–8.18 (m, 4H), 9.28 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 55.4, 114.5, 128.9, 129.0, 129.2, 129.3, 130.1, 141.2, 142.3, 143.0, 151.3, 161.4.

2-(4-Methylphenyl)quinoxaline (3e): Solid, m.p. 93–94 °C (lit.³³ 90–91 °C); ¹H NMR (300 MHz, CDCl₃): δ 2.44 (s, 3H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.71–7.77 (m, 2H), 8.09–8.16 (m, 4H), 9.30 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 21.3, 127.3, 129.0, 129.2, 129.4, 129.8, 130.1, 133.8, 140.4, 141.3, 142.2, 143.2, 151.7.

2-(4-Nitrophenyl)quinoxaline (3f): Solid, m.p. 188–191 °C (not reported);³⁴ ¹H NMR (300 MHz, DMSO-*d*₆): δ 7.90–7.93 (m, 2H), 8.13–8.16 (m, 2H), 8.39–8.42 (m, 2H), 8.56–8.59 (m, 2H), 9.67 (s, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 124.6, 129.2, 129.36, 129.9, 131.4, 131.5, 141.8, 142.0, 142.4, 144.4, 148, 9, 149.4.

2-(2-Chlorophenyl)quinoxaline (3g): Solid, m.p. 86–88 °C (not reported);³⁵ ¹H NMR (300 MHz, CDCl₃): δ 7.45–7.48 (m, 2H), 7.55–7.74 (m, 2H), 7.81–7.84 (m, 2H), 8.16–8.19 (m, 2H), 9.22 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 127.4, 129.1, 129.5, 130.1, 130.2, 130.2, 130.7, 131.8, 132.5, 136.4, 141.2, 142.2, 146.1, 152.3.

2-Methyl-3-phenylquinoxaline (3h): Solid, m.p. 54–56 °C (lit.¹¹ 56 °C); ¹H NMR (300 MHz, CDCl₃): δ 2.77 (s, 3H), 7.48–7.52 (m, 3H), 7.63–7.66 (m, 4H), 7.69–7.73 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): 24.3, 128.2, 128.5, 128.8, 128.9, 129.1, 129.2, 129.7, 138.9, 140.9, 141.1, 152.4, 154.8.

2-(2-Furanyl)quinoxaline (3i): Solid, m.p. 98–99 °C (lit.³³ 97–98 °C); ¹H NMR (300 MHz, CDCl₃): δ 6.61–6.62 (m, 1H), 7.30–7.31 (m, 1H), 7.67–7.75 (m, 3H), 8.04–8.10 (m, 2H), 9.23 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 111.8, 112.5, 129.2, 129.2, 129.3, 130.5, 141.2, 142.0, 142.1, 143.8, 145.1, 151.5.

2-(4-Fluorophenyl)quinoxaline (3j): Solid, m.p. 120–122 °C (lit.³³ 120–121 °C); ¹H NMR (300 MHz, CDCl₃): δ 7.21–7.27 (m, 2H), 7.75–7.78 (m, 2H), 8.09–8.21 (m, 4H), 9.27 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 116.16 (d, ²*J*_{CF} = 21.3 Hz), 129.07, 129.43 (d, ³*J*_{CF} = 8.25 Hz), 129.46, 129.54, 130.36, 132.84 (d, ³*J*_{CF} = 3.45 Hz), 141.4, 142.1, 142.9, 150.7, 164.2 (d, ¹*J*_{CF} = 248.93 Hz).

6,7-Dimethyl-2-phenylquinoxaline (3k): Solid, m.p. 127–129 °C (lit.³³ 128–129 °C); ¹H NMR (300 MHz, CDCl₃): δ 2.49 (s, 6H), 7.49–7.55 (m, 3H), 7.84 (s, 1H), 7.89 (s, 1H), 8.14–8.18 (m, 2H), 9.21 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 20.3, 20.3, 127.3, 128.1, 128.6, 129.0, 129.8, 137.0, 140.1, 140.5, 140.7, 141.1, 142.3, 150.9.

6,7-Dimethyl-2-(4-chlorophenyl)quinoxaline (3l): Solid, m.p. 160–163 °C (not reported);^{36,37} ¹H NMR (300 MHz, CDCl₃): δ 2.49 (s, 6H), 7.49 (d, *J* = 8.57 Hz, 2H), 7.82 (s, 1H), 7.85 (s, 1H), 8.09 (d, *J* = 8.57 Hz, 2H), 9.15 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 20.3, 20.4, 128.1, 128.5, 128.5, 129.2, 135.4, 136.1, 140.4, 140.5, 141.0, 141.0, 141.8, 149.6.

6,7-Dimethyl-2-(4-bromophenyl)quinoxaline (3m): Solid, m.p. 140–142 °C (lit.³⁸ 141–142 °C); ¹H NMR (300 MHz, CDCl₃): δ 2.50 (s, 6H), 7.66 (d, *J* = 8.7 Hz, 2H), 7.83 (s, 1H), 7.86 (s, 1H), 8.03 (d, *J* = 8.7 Hz, 2H), 9.16 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 20.3, 20.4, 124.5, 128.1, 128.5, 128.8, 132.2, 135.9, 140.4, 140.6, 141.0, 141.1, 141.8, 149.7.

6,7-Dimethyl-2-(4-methoxyphenyl)quinoxaline (3n): Solid, m.p. 126–129 °C; ¹H NMR (300 MHz, CDCl₃): δ 2.48 (s, 6H), 3.89 (s, 3H), 7.06 (d, *J* = 8.57 Hz, 2H), 7.82 (s, 1H), 7.85 (s, 1H), 8.13 (d, *J* = 8.57 Hz, 2H), 9.17 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 20.2, 20.3, 55.3, 114.4, 128.0, 128.4, 128.7, 129.5, 139.5, 140.0, 140.58, 141.1, 142.0, 150.5, 161.1. MS (EI, 70 eV) *m/z* (%): 266 (*M*⁺ + 2, 2), 265 (*M*⁺ + 1, 19), 264 (*M*⁺, 100), 249 (32). Anal. Calcd for C₁₇H₁₆N₂O: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.29; H, 6.07; N, 10.65%.

6,7-Dimethyl-2-(4-nitrophenyl)quinoxaline (3o): Solid, m.p. 197–200 °C; ¹H NMR (300 MHz, CDCl₃): δ 2.54 (s, 6H), 7.88 (s, 1H), 7.91 (s, 1H), 8.33 (d, *J* = 9.11 Hz, 2H), 8.38 (d, *J* = 9.11 Hz, 2H), 9.26 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 20.4, 20.4, 124.2, 128.0, 128.2, 128.7, 141.1, 141.1, 141.5, 141.6, 141.8, 142.9, 148.2, 148.5. MS (EI, 70 eV) *m/z* (%): 281 (*M*⁺ + 3, 2), 280 (*M*⁺ + 1, 19), 279 (*M*⁺, 100), 103 (42). Anal. Calcd for C₁₆H₁₃N₃O₂: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.87; H, 4.72; N, 15.09%.

6,7-Dimethyl-2-(2-chlorophenyl)quinoxaline (3p): Solid, m.p. 96–98 °C; IR (KBr) *v*_{max}/cm⁻¹: 3044, 2917, 1736, 1482, 1439, 1035, 755; ¹H NMR (300 MHz, CDCl₃): 2.50–2.51 (m, 6H), 7.40–7.44 (m, 2H), 7.51–7.52 (m, 1H), 7.69–7.72 (m, 1H), 7.89–7.91 (m, 2H), 9.10 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 20.3, 20.4, 127.1, 127.3, 128.1, 128.5, 130.1, 130.5, 131.8, 132.5, 136.7, 140.2, 140.8, 141.1, 145.1, 151.3; MS (EI, 70 eV) *m/z* (%): 270 (*M*⁺ + 2, 26), 268 (*M*⁺, 72), 233 (100), 134 (15), 103 (28). Anal. Calcd for C₁₆H₁₃ClN₂: C, 71.51; H, 4.88; N, 10.42. Found: C, 71.64; H, 4.96; N, 10.27%.

2,6,7-Trimethyl-3-phenylquinoxaline (3q): Solid, m.p. 92–95 °C (not reported);³⁹ ¹H NMR (300 MHz, CDCl₃): δ 2.48 (s, 3H), 2.49 (s, 3H), 2.75 (s, 3H), 7.48–7.52 (m, 3H), 7.63–7.66 (m, 2H), 7.80 (s, 1H), 7.86 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 20.3, 20.4, 24.2, 127.3, 128.2, 128.4, 128.7, 128.9, 139.3, 139.5, 139.9, 140.1, 140.1, 151.3, 153.8.

6,7-Dichloro-2-phenylquinoxaline (3r): Solid, m.p. 153–156 °C (not reported);⁴⁰ ¹H NMR (300 MHz, CDCl₃): δ 7.58–7.61 (m, 3H), 8.19–8.22 (m, 2H), 8.26 (s, 1H), 8.30 (s, 1H), 9.34 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 127.6, 129.3, 129.8, 130.2, 130.8, 134.1, 136.1, 140.3, 141.1, 144.3, 152.7.

6,7-Dichloro-2-(4-methoxyphenyl) quinoxaline (3s): Solid, m.p. 199–201 °C; IR (KBr) *v*_{max}/cm⁻¹: 2920, 2417, 1460, 1260, 1180, 1114, 837; ¹H NMR (300 MHz, CDCl₃): δ 3.92 (s, 3H), 7.1 (d, *J* = 8.8 Hz, 2H), 8.16 (d, *J* = 8.8 Hz, 2H), 8.19 (s, 1H), 8.22 (s, 1H), 9.27 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 55.5, 114.7, 128.4, 129.1, 129.7, 129.9, 133.3, 134.7, 139.9, 141.1, 144.0, 152.2. 161.9; MS (EI, 70 eV) *m/z* (%): 308 (*M*⁺ + 4, 11), 306 (*M*⁺ + 2, 63), 304 (*M*⁺, 100), 289 (21), 133 (19). Anal. Calcd for C₁₅H₁₀Cl₂N₂O: C, 59.04; H, 3.30; N, 9.18. Found: C, 59.16; H, 3.43; N, 9.27%.

6,7-Dichloro-2-(4-nitrophenyl) quinoxaline (3t): Solid, m.p. 223–225 °C; IR (KBr) *v*_{max}/cm⁻¹: 2921, 2398, 1733, 1458, 1348, 1110, 859; ¹H NMR (300 MHz, acetone-*d*₆): δ 8.39 (d, *J* = 8.7 Hz, 2H), 8.43 (s, 2H), 8.53 (d, *J* = 8.7 Hz, 2H), 9.68 (s, 1H); ¹³C NMR (75 MHz, acetone-*d*₆): δ 124.10, 128.86 (× 2), 130.02, 130.41, 134.08, 134.39, 140.92, 141.77, 145.04, 205.22, 205.48; MS (EI, 70 eV) *m/z* (%): 323 (*M*⁺ + 4, 11), 321 (*M*⁺ + 2, 62), 319 (*M*⁺, 100), 289 (26), 144 (22), 77 (32). Anal. Calcd for C₁₄H₇Cl₂N₃O₂: C, 52.53; H, 2.20; N, 13.13. Found: C, 52.41; H, 2.29; N, 13.22%.

6,7-Dichloro-2-(2-chlorophenyl)quinoxaline (3u): Solid, m.p. 113–115 °C; IR (KBr) *v*_{max}/cm⁻¹: 3048, 2918, 1453, 1316, 1112, 939, 752; ¹H NMR (300 MHz, CDCl₃): δ 7.46–7.57 (m, 3H), 7.70–7.72 (m, 1H), 8.28 (s, 1H), 8.29 (s, 1H), 9.22 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 127.6, 129.9, 130.2, 130.4, 131.2, 131.9, 132.5, 134.7, 134.9, 135.8, 140.0, 141.0, 147.1, 153.3; MS (EI, 70 eV) *m/z* (%): 314 (*M*⁺ + 6, 3), (312 (*M*⁺ + 4, 24), 310 (*M*⁺ + 2, 68), 308 (*M*⁺, 77), 275 (52), 273 (100), 109 (35). Anal. Calcd for C₁₄H₇Cl₃N₂: C, 54.32; H, 2.28; N, 9.05. Found: C, 54.49; H, 2.17; N, 8.96%.

2-Methyl-6,7-dichloro-3-phenylquinoxaline (3v): Solid, m.p. 151–153 °C (not reported);³⁹ ¹H NMR (300 MHz, CDCl₃): δ 2.78 (s, 3H), 7.54–7.56 (m, 3H), 7.64–7.65 (m, 2H), 8.17 (s, 1H), 8.23 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 24.5, 128.6, 128.96, 129.1, 129.4, 129.8, 133.6, 134.1, 138.2, 139.7, 139.9, 154.0, 155.9.

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References

- G. Sakata, K. Makino and Y. Kuraswa, *Heterocycles*, 1988, **27**, 2481.
- A. Dell, D.H. William, H.R. Morris, G.A. Smith, J. Feeney and G.C.K. Roberts, *J. Am. Chem. Soc.*, 1975, **97**, 2497.
- C. Bailly, S. Echepare, F. Gago and M. Waring, *Anti-Cancer Drug Des.*, 1999, **15**, 291.
- A. Katoh, T. Yoshida and J. Ohkanda, *Heterocycles*, 2000, **52**, 911.
- K.R.J. Thomas, M. Velusamy, J.T. Lin, C.H. Chuen and Y.T. Tao, *Chem. Mater.*, 2005, **17**, 1860.
- S. Dailey, W.J. Feast, R.J. Peace, I.C. Sage, S. Till and E.L. Wood, *J. Mater. Chem.*, 2001, **11**, 2238.
- O. Sascha and F. Rüdiger, *Synlett*, 2004, 150.
- J.L. Sessler, H. Maeda, T. Mizuno, V.M. Lynch and H. Furuta, *J. Am. Chem. Soc.*, 2002, **124**, 13474.
- M.J. Crossley and L.A. Johnston, *Chem. Commun.*, 2002, 1122.
- R.S. Bhosale, S.R. Sarda, S.S. Andhapure, W.N. Jadhav, S.R. Bhusare and R.P. Pawar, *Tetrahedron Lett.*, 2005, **46**, 7183.
- S.V. More, M.N.V. Sastry and C.-F. Yao, *Green Chem.*, 2006, **8**, 91.
- S.A. Raw, C.D. Wilfred and R.J.K. Taylor, *Org. Biomol. Chem.*, 2004, **2**, 788.
- S.Y. Kim, K.H. Park and Y.K. Chung, *Chem. Commun.*, 2005, 1321.
- R.S. Robinson and R.J.K. Taylor, *Synlett*, 2005, 1003.
- D. Aparicio, O.A. Attanasi, P. Filippone, R. Ignacio, S. Lillini, F. Mantellini, F. Palacios and J.M. de los Santos, *J. Org. Chem.*, 2006, **71**, 5897.
- C. Venkatesh, B. Singh, P.K. Mahata, H. Ila and H. Junjappa, *Org. Lett.*, 2005, **7**, 2169.
- S. Antoniotti and E. Duñach, *Tetrahedron Lett.*, 2002, **43**, 3971.
- Z. Wu and N.J. Ede, *Tetrahedron Lett.*, 2001, **42**, 8115.
- S.K. Singh, P. Gupta, S. Duggineni and B. Kundu, *Synlett*, 2003, 2147.
- J.F. Zhou, G.X. Gong, L.T. An and Y. Liu, *Synlett*, 2008, 3163.
- Y. Vara, E. Aldaba, A. Arrieta, J.L. Pizarro and M.I. Arriortua, *Org. Biomol. Chem.*, 2008, **6**, 1763.

- 22 B. Das, K. Venkateswarlu, K. Suneel and A. Majhi, *Tetrahedron Lett.*, 2007, **48**, 5371.
- 23 D.J. Zhu, J.X. Chen, M.C. Liu, D.C. Ding and H.Y. Wu, *J. Braz. Chem. Soc.*, 2009, **20**, 482.
- 24 J.X. Chen, H.Y. Wu, C. Jin, X.X. Zhang, Y.Y. Xie and W.K. Su, *Green Chem.*, 2006, **8**, 330.
- 25 J.X. Chen, H.Y. Wu, Z.G. Zheng, C. Jin, X.X. Zhang and W.K. Su, *Tetrahedron Lett.*, 2006, **47**, 5383.
- 26 W.K. Su, J.X. Chen, H.Y. Wu and C. Jin, *J. Org. Chem.*, 2007, **72**, 4524.
- 27 X.A. Chen, C.F. Zhang, H.Y. Wu, X.C. Yu, W.K. Su and J. Cheng, *Synthesis*, 2007, 3233.
- 28 J.X. Chen, W.K. Su, H.Y. Wu, M.C. Liu and C. Jin, *Green Chem.*, 2007, **9**, 972.
- 29 J.X. Chen, D.Z. Wu, F. He, M.C. Liu, H.Y. Wu, J.C. Ding and W.K. Su, *Tetrahedron Lett.*, 2008, **49**, 3814.
- 30 W.X. Guo, J.X. Chen, D.Z. Wu, J.C. Ding, F. Chen and H.Y. Wu, *Tetrahedron*, 2009, **65**, 5240.
- 31 H.M. Zheng, Q. Zhang, J.X. Chen, M.C. Liu, S.H. Cheng, J.C. Ding, H.Y. Wu and W.K. Su, *J. Org. Chem.*, 2009, **74**, 943.
- 32 H.L. Xiao, J.X. Chen, M.C. Liu, D.J. Zhu, J.C. Ding and H.Y. Wu, *Chem. Lett.*, 2009, **38**, 170.
- 33 C.S. Choa and S.G. Oh, *J. Mol. Catal. A: Chem.*, 2007, **276**, 205.
- 34 M.H. Rao, A.P.R. Reddy and V. Veeranaiaiah, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, 1992, **31B**, 88.
- 35 H. Inoue, M. Takeda, K. Higaki and H. Kugita, *Yakugaku Zasshi*, 1965, **85**, 95.
- 36 C.S. Cho, W.X. Ren and S.C. Shim, *Tetrahedron Lett.*, 2007, **48**, 4665.
- 37 B. Insuasty, F. Fernandez, J. Quiroga, R. Moreno and R. Abonia, *Heterocycl. Commun.*, 2002, **8**, 259.
- 38 A.I. Zbruyev, F.G. Yaremenko, V.A. Chebanov, S.M. Desenko, O.V. Shishkin, E.V. Lukinova and I.V. Knyazeva, *Russ. Chem. Bull.*, 2006, **55**, 362.
- 39 C.S. Mahajanshetti and M.N. Balse, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, 1978, **16B**, 830.
- 40 A. Gazit, H. App, G. McMahon, J. Chen, A. Levitzki and F.D. Bohmer, *J. Med. Chem.*, 1996, **39**, 2170.

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