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NOVEL HIGHLY REGIOSELECTIVE SYNTHESSES OF UNSYMMETRICAL 2,3-DISUBSTITUTED QUINOXALINES#

**Xu Hui,¹ Fanny Schmidt, Mohammed Akram Fakhfakh, Xavier Franck, and
Bruno Figadère***

**Laboratory of Pharmacognosy (associated to the CNRS, UMR-8076-BioCIS),
University of Paris-Sud 11, Faculty of Pharmacy, rue J.-B. Clément, F-92296
Châtenay-Malabry, France**

E-mail: bruno.figadere@cep.u-psud.fr

Abstract – Non-symmetrical 2,3-disubstituted quinoxalines are not easily obtained in good yields because of the lack of regioselectivity of the Hinsberg condensation, or the large number of steps required for achieving their preparation. Two efficient methods leading to non-symmetrical 2,3-disubstituted quinoxalines, carried out in smooth conditions, have been developed in our laboratory. These methods enable the synthesis of pharmacologically active quinoxaline derivatives.

INTRODUCTION

Nitrogen-containing heterocyclic compounds are an important class of pharmacologically active products, among which quinoxalines display a broad spectrum of activities.¹ They also find applications in organic semiconductors,² dyes,³ and electroluminescent materials.⁴ A number of synthetic methods have been developed for the synthesis of substituted quinoxalines, and the probably most widely used one is the Hinsberg condensation of an aryl 1,2-diamine with 1,2-dicarbonyl compounds in refluxing ethanol or acetic acid.⁵ Some improved reaction conditions have then been reported, such as the use of catalysts,⁶ microwaves,⁷ and solid supports synthesis.⁸ However, the lack of regioselectivity leading to the formation of regioisomeric products with unsymmetrically substituted reactants, is the major drawback of this method.⁹ Thus various regioselective routes to unsymmetrical quinoxalines were reported but suffer from

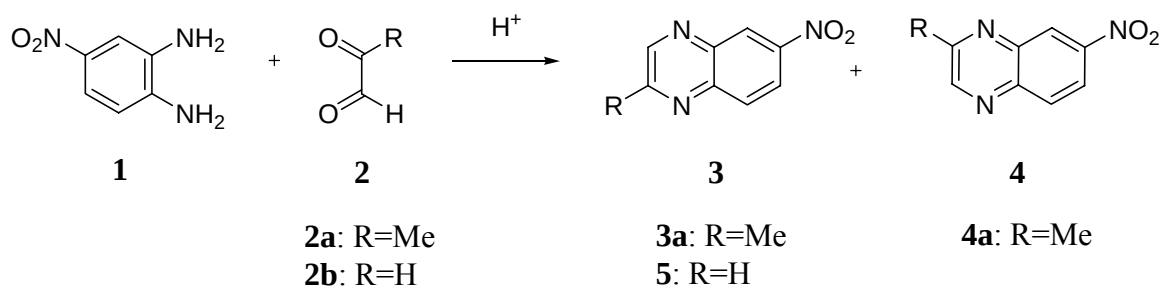
#This paper is dedicated to Pr. Yoshito Kishi with a deep respect and admiration for his outstanding achievements in the field of total synthesis of natural products.

¹ New address : College of Life Science, Northwest Sci-Tec University of Agriculture and Forestry, China.

limited scope, vigorous conditions and low yields.¹⁰ During the course of our ongoing research on the preparation and the study of the biologically properties of quinoxalines and derivatives,¹¹ we have developed efficient routes to 6-amino-2,3-dialkylquinoxalines through the direct addition of organolithium reagents to 6-aminoquinoxaline.

RESULTS AND DISCUSSION

Miocque *et al.* have reported that butyllithium and phenyllithium add to 2-methylquinoxaline in diethyl ether to give a complex mixture of adducts, where the aromatized addition product could be isolated in low yield.¹² In order to prepare unsymmetrical 2,3-disubstituted-6-aminoquinoxalines we decided to re-investigate the addition of organolithium reagents to 2-methyl-6-aminoquinoxaline (**6**) and 6-aminoquinoxaline (**8**). Compound (**6**) was easily obtained by the regioselective Hinsberg condensation of 1,2-diamino-4-nitrobenzene (**1**) with pyruvic aldehyde (**2a**) leading to nitro-intermediates (**3a**) and (**4a**) in a 10:1 ratio (regioisomers were unambiguously identified by NMR analysis, *vide infra*). Reduction of (**3a**) (SnCl_2 , EtOH) gave 2-methyl-6-aminoquinoxaline (**6**). 6-Aminoquinoxaline (**8**) was prepared as well from 1,2-diamino-4-nitrobenzene (**1**) and glyoxal (**2b**), to give, after nitro-reduction of the intermediate (**5**), 6-aminoquinoxaline (**8**).

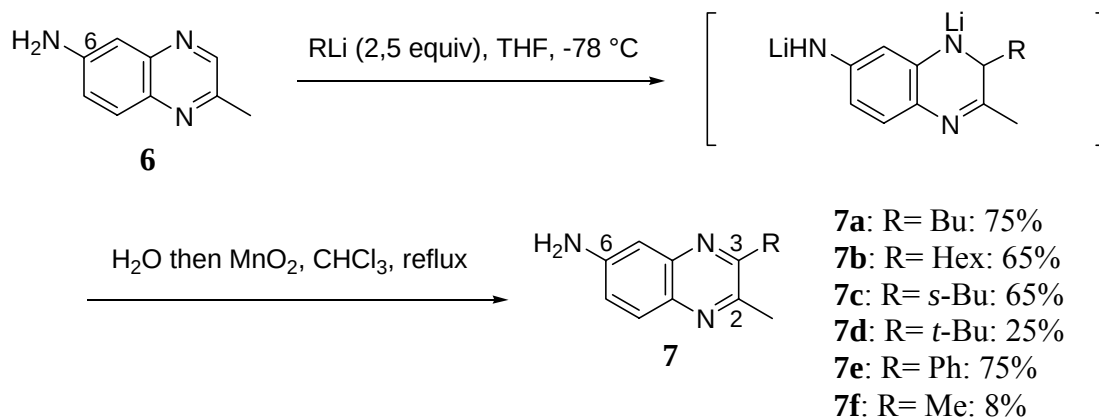


When R= Me : **3/4** $\Rightarrow$ 10 : 1, yield 90% ; When R= H : **5**, yield 95%

Scheme 1. Hinsberg condensation of 1,2-diamino-4-nitrobenzene (**1**) with methylpyruvaldehyde (**2a**) and glyoxal (**2b**)

Then, when 2-methyl-6-aminoquinoxaline (**6**) reacted with butyllithium in THF at -78°C , the expected 1,2-alkylated adduct was obtained but not isolated, instead it was directly oxidized by MnO_2 to the corresponding 3-butyl-2-methyl-6-aminoquinoxaline (**7a**) in a satisfying 75% overall yield. Then several other organolithium reagents were used under the similar reaction conditions and afforded the expected

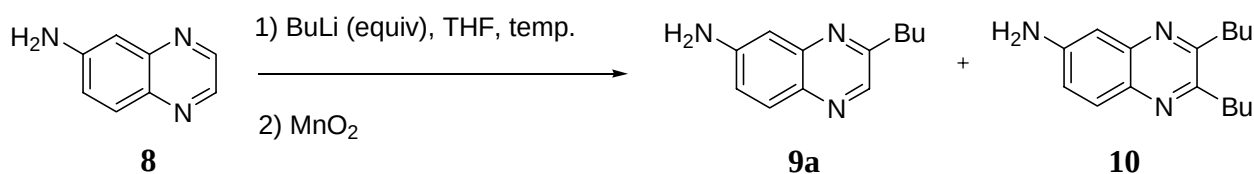
coupled products (**7b-f**) in good yields (Scheme 2), except for (**7d**) and (**7f**). Not surprisingly, when *t*-butyllithium or methyllithium were used, moderate yields of the expected quinoxalines were obtained.



Scheme 2. Organolithium addition to 2-methyl-6-aminoquinoxaline (**6**)

We then decided to carry out the addition of butyllithium to 6-aminoquinoxaline (**8**) (Table 1, entry 1), and were delighted to observe that, after re-oxidation by MnO_2 of the intermediate, the 3-substituted product (**9a**) was obtained, but in a moderate 54% yield, when the reaction was performed with 2.5 equiv. of butyllithium at $-78\text{ }^\circ\text{C}$ in THF (Table 1, entry 2). If a larger excess of butyllithium was used (3 equiv., entry 3), the disubstituted product (**10**) was now obtained in 18% yield, together with the expected mono-substituted adduct (**9a**), albeit in lower yield (45%).

Table 1. Synthesis of 3-butyl-6-aminoquinoxaline (**9a**)

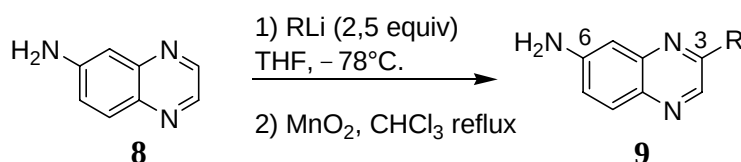


Entry	BuLi (equiv)	Temp. ($^\circ\text{C}$)	9a Yield (%)	10 Yield (%)
1	1.5	-78	25	0
2	2.5	-78	54	2
3	3	-78	45	18
4	2.5	-78 to 0	NR ^a	-
5	2.5	0	30	23
6	3	0	11	54
7	BuMgCl	0	Traces	-

a) in Et_2O , NR :no reaction

If the reaction was run in diethyl ether, no reaction occurred, even at 0 °C (entry 4). When the reaction was run in THF at 0 °C, a mixture of mono- and disubstituted products (**9a**) and (**10**) was now obtained (entry 5). However, when a large excess of BuLi was used (3 equiv, entry 6) and the temperature maintained at 0 °C, the disubstituted product (**10**) was now obtained as the major product in a moderate 54% yield, together with the mono-substituted product (**9a**) albeit in low yield (11%). Finally, when a Grignard reagent was used, only trace amounts of the mono-adduct (**9a**) could be isolated (entry 7). The regioselectivity could tentatively be rationalized by invoking a complex formed between lithium amide of the quinoxaline and the organolithium reagent, that will attack position 3 of (**8**). Nevertheless, more experiments are needed in order to better explain the observed selectivity. In order to study the scope and limitation of this reaction, other organolithium reagents were used ; for primary alkyl reagents, the expected products (**9a,b**) were obtained in moderate yields (see Table 2). With secondary and tertiary alkyl lithium reagents, the mono-adducts (**9c**) and (**9d**) were obtained in 40% and 26% yield (entries 3 and 4), respectively. With phenyllithium, low yield was also obtained in the expected product (**9e**) (28%), whereas no reaction occurred with methyllithium.

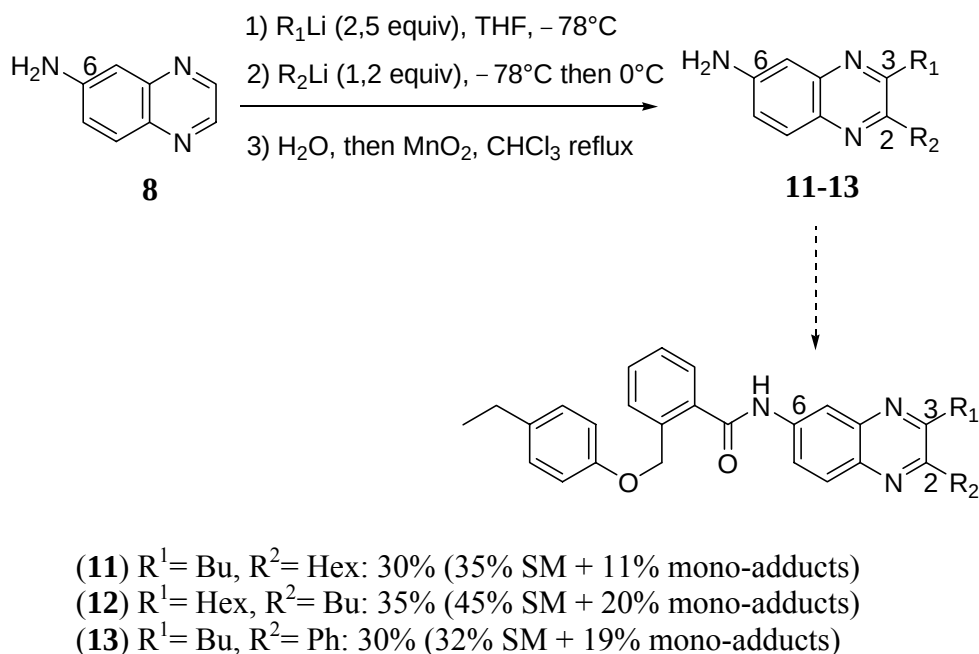
Table 2. Synthesis of 3-substituted-6-aminoquinoxalines (**9**) from 6-aminoquinoxaline (**8**)



entry	RLi	Product	Yield (%)
1	Bu	9a	54
2	Hex	9b	53
3	<i>s</i> -Bu	9c	40
4	<i>t</i> -Bu	9d	26
5	Ph	9e	28
6	Me	9f	no reaction

Finally, we decided to study the addition of organolithium reagents to 3-butyl-6-aminoquinoxaline (**9a**). Surprisingly when hexyllithium was added to (**9a**) in THF at −78 °C, and after re-oxidation by MnO₂ of the intermediate, expected 3-butyl-2-hexyl-6-aminoquinoxaline (**11**) was obtained only in traces amount, even when the temperature was allowed to reach rt (result not shown). We thus decided to study the one-pot reaction with two different organolithium reagents, in order to prepare unsymmetrical

2,3-disubstituted-6-aminoquinoxalines (Scheme 3).



Scheme 3. Double organolithium addition to 6-aminoquinoxaline (**8**)

Thus, when 6-aminoquinoxaline (**8**) was first treated by butyllithium at $-78^\circ C$, followed by hexyllithium at $0^\circ C$, and oxidation of the crude mixture by MnO_2 , the expected product (**11**) was obtained in 30% yield, with recovery of the starting material (35%) and the two mono-adducts (11%). Whereas, when hexyllithium was first added to (**8**) at $-78^\circ C$, followed by butyllithium at $0^\circ C$, then oxidation, the regioisomer (**12**) was now obtained in 35% yield, with the starting material (45%) and the two mono-adducts (20%). Surprisingly, when 6-aminoquinoxaline (**8**) was first treated with butyllithium then phenyllithium, the product (**13**) was obtained in 30% yield, and the starting material recovered in about the same proportions. In fact, the observed overall yields of 30% for (**11-13**) refer to one deprotonation, two new C-C bond formations, two oxidation reactions sequence, and are thus quite satisfying. It is also note worthy that the second addition of organolithium reagent at position 3 of the dihydro-quinoxaline intermediate is probably easier because of aromaticity of the heterocycle no longer exists, and this may explain why the addition of hexyllithium to 3-butyl-6-aminoquinoxaline (**9a**) failed.

In conclusion, we have shown that 3-alkyl-6-aminoquinoxalines (**9a-f**) are easily obtained by direct alkylation of 6-aminoquinoxaline (**8**). Then unsymmetrical 2,3-dialkylated-6-aminoquinoxalines can be easily prepared either by mono-alkylation of 2-methyl-6-aminoquinoxaline (**6**), or by a regioselective double alkylation of 6-aminoquinoxaline (**8**). These methods are complementary to the Hinsberg condensation, that produces the opposite regioisomer when regioselectivity is observed. These new

methods will surely find applications in the preparation of pharmacologically active compounds that possess quinoxaline pharmacophore, such as the amide represented in Scheme 3 that shows some leishmanicidal activity,^{11c} whose biological properties will be published elsewhere.

EXPERIMENTAL

General. Solvents were purified according to the procedures described.¹³ Reagent grade 1,2-diamino-4-nitrobenzene (**1**), aldehydes (**2a,b**) were purchased and directly used. THF, Et₂O were distilled over sodium-benzophenone. Yields were calculated from aminoquinoxalines (**6**) and (**8**) for material after purification by flash column chromatography. Thin-layer chromatography was performed on Meck Kieselgel 60F254 plates, eluting with the solvents indicated and visualized by a 366 nm UV lamp, and stained with an ethanolic solution of sulfuric vanillin. Flash column chromatography was performed with silica gel (Riedel-de Haën, 230-400 mesh) and eluted with indicated solvents. Nuclear magnetic resonance (NMR) spectra were acquired at either 400, 300 or 200 MHz for ¹H and 50 MHz for ¹³C, and described according to Hoye.¹⁴ Glassware for all reactions was dried at 100 °C and cooled under a nitrogen atmosphere prior to use. Reagents and solvents were introduced by oven dried syringes through septa sealed flasks under nitrogen atmosphere.

Synthesis of 2-methyl-6-nitroquinoxaline (**3a**):

A mixture of 1,2-diamino-4-nitrobenzene (3.06g, 20 mmol) and pyruvic aldehyde (3.6 mL, 20 mmol, 40% in H₂O) in H₂O (50 mL) was heated to 90 °C for 1.5 h under nitrogen. After cooling, solid was obtained by filtration, washed by water, dissolved in CH₂Cl₂, dried over anhydrous MgSO₄ and concentrated *in vacuo* to give a brown-orange solid (90%). ¹H-NMR (400MHz, CDCl₃) δ ppm: 2.82 (s, 3H); 8.10 (d, J = 8.4Hz, 1H); 8.45 (d, J = 8.0Hz, 1H); 8.87 (s, 1H); 8.92 (s, 1H). ¹³C-NMR (50MHz, CDCl₃) δ ppm: 22.8; 123.3; 125.5; 130.2; 139.7; 144.5; 147.0; 148.1; 157.3. ESI-MS m/z: 190 (M+H⁺, 100). IR cm⁻¹: 715, 745, 795, 830, 860, 930, 940, 965, 1080, 1185, 1210, 1295, 1340, 1390, 1455, 1490, 1520, 1565, 1615, 2955, 3045.

Synthesis of 6-nitroquinoxaline (**5**):

Glyoxal (2.8 mL, 24 mmol, 40% in H₂O) was added dropwise to a solution of 4-nitro-phenylene-1,2-diamine (1.53g, 10 mmol) in H₂O (30 mL). The mixture was heated to 100 °C for 4 h under nitrogen. After cooling, the solid was obtained by filtration, then washed with water, dissolved in CH₂Cl₂, dried over MgSO₄ and concentrated *in vacuo* to give an orange solid (93%). ¹H-NMR (400MHz, CDCl₃) δ ppm: 8.26 (d, J = 9.2Hz, 1H); 8.52 (dd, J = 9.2Hz, J = 2.4Hz, 1H); 9.01 (s, 3H). ¹³C-NMR (50MHz, CDCl₃) δ ppm: 123.4; 125.9; 131.3; 141.9; 145.3; 147.0; 147.6; 147.9. ESI-MS m/z: 176 (M+H⁺, 23). IR cm⁻¹: 740, 810, 850, 870, 930, 955, 1020, 1075, 1130, 1190, 1205, 1295, 1345, 1370, 14209, 1445, 1490, 1520, 1545, 1585, 1610, 3055, 3090.

General procedure for synthesis of 2-methyl-6-aminoquinoxaline (**6**) and 6-aminoquinoxaline (**8**):

Compound (**3**) or (**5**) (20 mmol) and SnCl₂ (1.89 g, 100 mmol) diluted in absolute ethanol (50 mL) was refluxed for 4h under nitrogen. The reaction mixture was basified to pH 8 with saturated NaHCO₃ and the solution was filtered through celite to remove the precipitate, and washed with EtOAc. The organic layers were separated and the water layer was extracted three times with EtOAc. The combined organic layers

were washed with brine, dried over anhydrous MgSO_4 and concentrated *in vacuo* to give the products. Compound **(8)** (80%): $^1\text{H-NMR}$ (400MHz, CDCl_3) δ ppm: 4.10 (s, 2H); 7.12 (d, $J = 2.4\text{Hz}$, 1H); 7.15 (dd, $J = 8.8\text{Hz}$, $J = 2.4\text{Hz}$, 1H); 7.84 (d, $J = 8.8\text{Hz}$, 1H); 8.52 (s, 1H); 8.62 (s, 1H). $^{13}\text{C-NMR}$ (50MHz, CDCl_3) δ ppm: 148.1; 144.9; 140.9; 137.9; 130.3; 122.0; 107.8. ESI-MS m/z : 146 ($\text{M}+\text{H}^+$, 100). IR cm^{-1} : 3395, 3315, 3185, 3055, 1645, 1615, 1545, 1500, 1470, 1435, 1370, 1310, 1225, 1210, 1135, 1030, 960, 860, 815, 765. Compound **(6)** (80%): $^1\text{H-NMR}$ (300MHz, CDCl_3) δ ppm: 2.62 (s, 3H); 4.22 (s, 2H); 7.09-7.11 (m, 2H); 7.73 (d, $J = 4.2\text{Hz}$, 1H); 8.52 (s, 1H). $^{13}\text{C-NMR}$ (75MHz, CDCl_3) δ ppm: 149.3; 147.1; 145.7; 142.5; 141.7; 136.8; 129.4; 121.7; 108.1; 21.8. ESI-MS m/z : 160 ($\text{M}+\text{H}^+$, 100). IR cm^{-1} : 3330, 3205, 3055, 2920, 1615, 1555, 1500, 1475, 1420, 1365, 1345, 1310, 1230, 1210, 1170, 1130, 1015, 970, 940, 910, 830, 780, 755, 730.

General procedure for synthesis of 3-substituted-2-methyl-6-aminoquinoxaline (7a-7e) and 3-substituted-6-aminoquinoxaline (9a-9e).

Organolithium reagent (2.5 mmol) was added dropwise to a solution of compound **(6)** or **(8)** (1 mmol) in anhydrous THF at -78°C under nitrogen. The mixture was stirred at -78°C for 2.5 h, then quenched by NH_4Cl , extracted with EtOAc , washed with brine, dried over anhydrous MgSO_4 and concentrated *in vacuo*. The residue was dissolved in CHCl_3 (20 mL), MnO_2 (440 mg, 5 mmol) was added and the mixture was refluxed for 4h. The reaction was quenched with water (2 mL) and filtered through celite to remove the residues, dried over MgSO_4 and concentrated *in vacuo*. The products were purified by column chromatography to give compounds **(7a)** to **(7f)** and **(9a)** to **(9f)**. Compound **(7a)**: $^1\text{H-NMR}$ (300MHz, CDCl_3) δ ppm: 0.98 (t, $J = 7.2\text{Hz}$, 3H); 1.47 (m, 2H); 1.77 (m, 2H); 2.90 (t, $J = 7.8\text{Hz}$, 2H); 4.04 (s, 2H); 7.07 (m, 2H); 7.75 (d, $J = 8.1\text{Hz}$, 1H). $^{13}\text{C-NMR}$ (75MHz, CDCl_3) δ ppm: 13.9; 22.3; 22.8; 30.5; 35.7; 108.1; 120.5; 129.1; 135.7; 142.7; 146.9; 148.9; 156.9. ESI-MS m/z : 216 ($\text{M}+\text{H}^+$, 100). IR cm^{-1} : 705, 740, 780, 790, 830, 855, 875, 955, 970, 1010, 1075, 1105, 1130, 1160, 1250, 1285, 1315, 1345, 1375, 1460, 1500, 1555, 1620, 1655, 2870, 2925, 2955, 3170, 3320. Compound **(7b)**: $^1\text{H-NMR}$ (300MHz, CDCl_3) δ ppm: 0.89 (t, $J = 6.6\text{Hz}$, 3H); 1.25-1.60 (m, 8H); 2.68 (s, 3H); 2.92 (t, $J = 8.1\text{Hz}$, 2H); 4.05 (s, 2H); 7.06 (m, 2H); 7.77 (d, $J = 8.4\text{Hz}$, 1H). $^{13}\text{C-NMR}$ (75MHz, CDCl_3) δ ppm: 14.0; 22.3; 22.6; 28.4; 29.4; 31.6; 108.2; 120.5; 129.16; 135.7; 142.8; 146.9; 148.8; 156.9. ESI-MS m/z : 244 ($\text{M}+\text{H}^+$, 100). IR cm^{-1} : 830, 1005, 1080, 1135, 1240, 1345, 1375, 1465, 1500, 1545, 1585, 1620, 1690, 2005, 2145, 2345, 2360, 2855, 2925, 2955, 3225, 3340. Compound **(7c)**: $^1\text{H-NMR}$ (300MHz, CDCl_3) δ ppm: 0.89 (t, $J = 7.5\text{Hz}$, 3H); 1.32 (d, $J = 6.9\text{Hz}$, 3H); 1.63 (m, 1H); 1.92 (m, 1H); 2.69 (s, 3H); 3.14 (q, $J = 6.9\text{Hz}$, 1H); 4.02 (s, 2H); 7.09 (m, 2H); 7.74 (d, $J = 8.7\text{Hz}$, 1H). $^{13}\text{C-NMR}$ (75MHz, CDCl_3) δ ppm: 12.3; 19.3; 22.4; 28.9; 38.9; 108.5; 120.5; 129.0; 135.3; 140.6; 146.8; 148.7; 160.7. ESI-MS m/z : 216 ($\text{M}+\text{H}^+$, 100). IR cm^{-1} : 730, 830, 855, 910, 1000, 1020, 1050, 1075, 1130, 1180, 1235, 1320, 1375, 1460, 1500, 1555, 1620, 2360, 2870, 2925, 2960, 3220, 3345. Compound **(7d)**: $^1\text{H-NMR}$ (300MHz, CDCl_3) δ ppm: 1.51 (s, 9H); 2.84 (s, 3H); 4.22 (s, 2H); 7.09 (m, 2H); 7.73 (d, $J = 9.0\text{Hz}$, 1H). $^{13}\text{C-NMR}$ (75MHz, CDCl_3) δ ppm: 25.7; 29.4; 108.8; 120.7; 128.7; 134.9; 141.5; 146.8; 148.4; 1

108.0; 120.7; 130.0; 136.1; 141.8; 144.0; 147.9; 157.7. ESI-MS m/z : 230 ($M+H^+$, 100). IR cm^{-1} : 730, 775, 830, 905, 975, 1080, 1135, 1160, 1185, 1235, 1280, 1340, 1370, 1465, 1510, 1550, 1620, 2360, 2855, 2925, 2955, 3215, 3340. Compound (**9c**): 1H -NMR (300MHz, $CDCl_3$) δ ppm: 0.90 (t, J = 7.5Hz, 3H); 1.37 (d, J = 7.2Hz, 3H); 1.73 (m, 1H); 1.88 (m, 1H); 2.96 (m, 1H); 4.12 (s, 2H); 7.09 (m, 2H); 7.84 (d, J = 9.6Hz, 1H); 8.45 (s, 1H). ^{13}C -NMR (75MHz, $CDCl_3$) δ ppm: 12.1; 19.9; 29.6; 42.1; 108.1; 120.7; 130.0; 136.3; 141.0; 144.0, 147.8; 161.4. ESI-MS m/z : 202 ($M+H^+$, 100). IR cm^{-1} : 735, 775, 830, 855, 905, 960, 980, 1015, 1050, 1085, 1130, 1175, 1230, 1250, 1275, 1370, 1430, 1460, 1510, 1545, 1620, 2360, 2875, 2925, 2960, 3215, 3340. Compound (**9d**): 1H -NMR (300MHz, $CDCl_3$) δ ppm: 1.44 (s, 9H); 4.21 (s, 2H); 7.05 (m, 1H); 7.78 (d, J = 9.3Hz, 1H); 8.67 (s, 1H). ^{13}C -NMR (75MHz, $CDCl_3$) δ ppm: 29.6; 36.9; 108.2; 120.7; 127.9; 135.6; 139.1; 143.2; 147.8; 163.6. ESI-MS m/z : 202 ($M+H^+$, 100). IR cm^{-1} : 730, 775, 830, 855, 905, 955, 975, 1020, 1110, 1200, 1245, 1280, 1365, 1430, 1460, 1505, 1545, 1620, 2960, 3215, 3335. Compound (**9e**): 1H -NMR (300MHz, $CDCl_3$) δ ppm: 4.12 (s, 2H); 7.08 (m, 2H); 7.45 (m, 3H); 7.82 (d, J = 9.6Hz, 1H); 8.08 (d, J = 9.5Hz, 2H); 8.95 (s, 1H).

General procedure for synthesis of 2, 3-disubstituted-6-aminoquinoxaline (**11** to **13**):

Organolithium reagent (2.5 mmol) was added dropwise to a solution of compounds (**6**) or (**8**) (1 mmol) in anhydrous THF at $-78^\circ C$ under nitrogen. The mixture was stirred at $-78^\circ C$ for 2.5 h, then the second organolithium reagent (2 mmol) was added, and the reaction mixture was warmed to $0^\circ C$ and stirred for 2 h. The reaction was quenched by NH_4Cl , extracted with EtOAc, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was dissolved in $CHCl_3$ (20 mL), MnO_2 (440 mg, 5 mmol) was added and the mixture was refluxed for 4 h. The reaction was quenched with water (2 mL) and filtered through celite to remove the residues, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The products were purified by column chromatography to give compounds (**11**) to (**13**). Compound (**11**): 1H -NMR (300MHz, $CDCl_3$) δ ppm: 0.96 (m, 6H); 1.31-1.32 (m, 8H); 1.40-1.52 (m, 2H); 1.68-1.79 (m, 2H); 2.9 (m, 4H); 4.10 (s, 2H); 7.05 (m, 2H); 7.74 (d, J = 9.6Hz, 1H). ^{13}C -NMR (75MHz, $CDCl_3$) δ ppm: 13.9; 14.0; 22.5; 29.1; 29.2; 29.3; 29.4; 31.6; 35.1; 35.4; 108.0; 120.5; 129.3; 135.8; 142.5; 146.9; 152.6; 156.6. ESI-MS m/z : 286 ($M+H^+$, 40). IR cm^{-1} : 725, 830, 855, 930, 960, 1080, 1135, 1235, 1340, 1465, 1500, 1620, 2925, 2855, 2955, 3215, 3335. Compound (**12**): 1H -NMR (300MHz, $CDCl_3$) δ ppm: 0.92 (m, 6H); 1.25-1.45 (m, 8H); 1.72-1.82 (m, 4H); 2.92 (m, 4H); 4.06 (s, 2H); 7.06 (m, 2H); 7.77 (d, J = 7.8Hz, 1H). ^{13}C -NMR (75MHz, $CDCl_3$) δ ppm: 13.9; 14.0; 22.5; 22.8; 29.0; 29.1; 29.4; 31.6; 35.1; 35.4; 108.0; 120.5; 129.2; 135.8; 142.5; 146.9; 152.5; 156.6. ESI-MS m/z : 286 ($M+H^+$, 100). IR cm^{-1} : 730, 830, 855, 905, 960, 1075, 1135, 1170, 1235, 1345, 1465, 1500, 1550, 1625, 2860, 2930, 2955, 3215, 3335. Compound (**13**): 1H -NMR (300MHz, $CDCl_3$) δ ppm: 0.82 (t, J = 7.2Hz, 3H); 1.25 (m, 4H); 1.67 (t, J = 7.8Hz, 2H); 2.95 (t, J = 7.8Hz, 2H); 4.15 (s, 2H); 7.13 (m, 2H); 7.43-7.58 (m, 5H); 7.88 (d, J = 8.7Hz, 1H). ^{13}C -NMR (75MHz, $CDCl_3$) δ ppm: 13.7; 22.6; 26.8; 31.3; 35.6; 107.5; 121.1; 128.0; 128.2; 128.3; 128.8; 129.6; 129.7; 130.1; 135.6; 139.5; 143.2; 147.7; 151.1; 156.2. ESI-MS m/z : 278 ($M+H^+$, 100). IR cm^{-1} : 730, 765, 830, 855, 910, 965, 1010, 1075, 1135, 1240, 1345, 1420, 1445, 1460, 1495, 1560, 1580, 1620, 2855, 2925, 2955, 3060, 3215, 3335.

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