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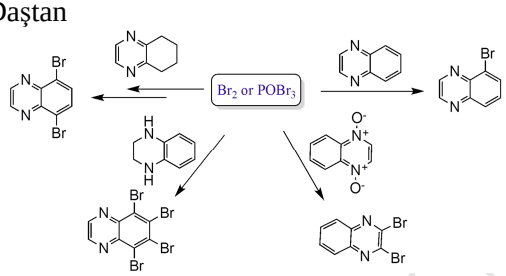

Bromination of Quinoxaline and Derivatives: Effective Synthesis of Some New Brominated Quinoxalines[†]

Sefa Uçar,[a] Selçuk Eşsiz[a,b] and Arif Daştan[a*]

Abstract— The synthesis of brominated quinoxaline derivatives starting from several kinds of quinoxaline by different bromination strategies was studied. First the synthesis of some brominated quinoxalines was accomplished along with the development of an alternative and effective synthesis of some known compounds. A new, clean, and effective synthetic method for selective reduction of quinoxaline to 1,2,3,4-tetrahydroquinoxaline was also developed. The products obtained were characterized by means of NMR spectroscopy, elemental analyses, and mass spectrometry.

Keywords: quinoxaline, tetrahydroquinoxaline, bromination, Birch reduction, aromatization

1. Introduction

The chemistry of benzenoid hydrocarbons such as naphthalene goes back to the 19th century.[1] Although many investigations have been performed on this kind of molecule, benzenoid hydrocarbons are still valuable due to their importance in both material sciences and medicinal chemistry. Two nitrogen-containing heteroaromatic naphthalene derivatives, called diazanaphthalene and naphthyridines or diazines, are important structures found in many natural and synthetic compounds.[2]

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[†]Electronic supplementary information (ESI) available. See DOI: 10.1039 xxxxxxx

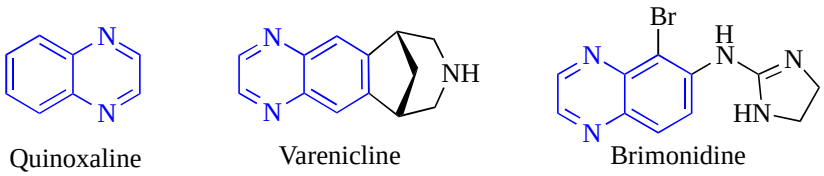


Figure 1 Quinoxaline and its derivatives

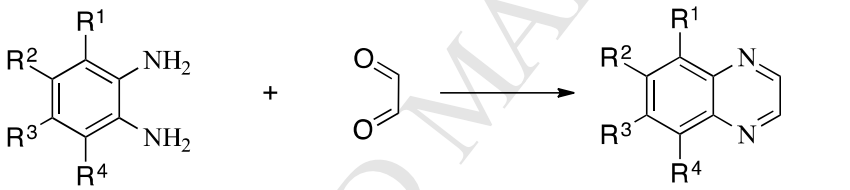
Among them, 1,4-diazanaphthalene, that is to say quinoxaline (**1**), is a crucial core structure of various macrocyclic antibiotics such as echinomycin,[3] levomycin,[4] and actinoleutin[5] that are known to inhibit growth of Gram-positive bacteria, and are active against various transplantable tumors. Even small analogues such as varenicline (**2**)[6] and brimonidine (**3**)[7] have valuable pharmaceutical effects. (Figure 1). In addition to biological and pharmaceutical effects, molecules consisting of a quinoxaline unit, have many important applications in material sciences. For example, quinoxaline derivatives are useful as electroluminescent materials,[8] organic semiconductors,[9] dyes,[10] and electrical/photochemical materials.[11] Their ability to harvest both singlet and triplet energy for emission improves device efficiency. For example, a few compounds with quinoxaline unit are used for dye-sensitized solar cells.[10b,12]

Consequently, significant efforts have been made to develop efficient methods for the synthesis of quinoxalines and their derivatives. The traditional method relies on condensation of 1,2-diamines with 1,2-dicarbonyl compounds,[13] while oxidative cyclization of α-hydroxy ketones or α-halide ketones with 1,2-diamines has also been widely used.[14] Although these methods work well for a few derivatives at routine positions, quinoxalines substituted in more specific positions suffer when the substituted 1,2-diamines and 1,2-dicarbonyl compounds are used as starting materials.

Furthermore, brominated compounds are versatile key compounds and starting materials for many organic transformations. Halogens may be reductively or permutationally replaced by lithium or magnesium, and the organometallic intermediate converted into a functionalized derivative by reaction with an appropriate electrophile. In addition, the C-Br bond formed in arenes can be easily transformed into a C-C bond and C–hetero atom bond via Ullmann, Heck, Stille, Suzuki etc. reactions.[15] For this reason, the synthesis of halogenated arenes is extremely important in organic chemistry and material science.

In our previous works, we examined the bromination of naphthalene and its derivatives and we obtained many new naphthalene derivatives.[16] Cakmak and co-workers also studied the bromination and

functionalization of benzenoid aromatic compounds such as naphthalene, anthracene, and quinoline.[17] Due to our sustained interest in the bromination of aromatic compounds and derivatives, we aimed to study quinoxalines to find a regioselective bromination method for the parent compounds. Although bromination of naphthalene has been investigated in detail by many groups,[16-18,] direct bromination of diazanaphthalenes is not common, owing to the lower activity of these compounds in electrophilic reactions. Diazanaphthalenes are electron-deficient in nature, and N-bromo complexes form easily during the bromination reaction. For this reason, direct bromination of quinoxaline has not been reported in the literature to achieve brominated products as key compounds for other kinds of functionalization. Brominated quinoxalines **9**,[19] **10**,[20] **11**,[21] and **12**[22] have been obtained by condensation of benzene-1,2-diamines **4-7** with glyoxal (**8**) (Scheme 1). Although the last step works well, synthesis of halogenated benzene-1,2-diamines in specific positions is not easy and consequently there are no practical and general methods for the synthesis of many halogenated derivatives. In addition, most of this conversion was patented.[20,21] Continuing our work on the bromine functionalization of hydrocarbons, herein we describe the halogenation of quinoxaline and derivatives under different conditions.



4 (R^1=Br, R^2=R^3=R^4=H)
5 (R^2=Br, R^1=R^3=R^4=H)
6 (R^1=R^3=Br, R^2=R^4=H)
7 (R^1=R^4=Br, R^2=R^3=H)

9 (R^1=Br, R^2=R^3=R^4=H)
10 (R^2=Br, R^1=R^3=R^4=H)
11 (R^1=R^3=Br, R^2=R^4=H)
12 (R^1=R^4=Br, R^2=R^3=H

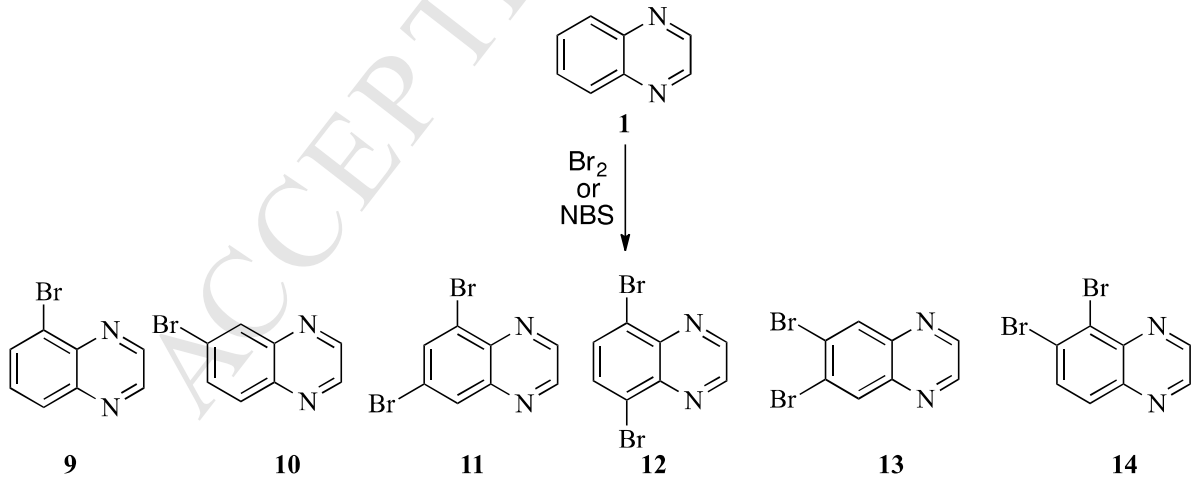
Scheme 1 Synthesis of some bromoquinoxalines

2. Results and Discussion

Our work in this study is based on three main strategies: i) bromination of quinoxaline (**1**) with different reagents, solvents, and temperatures, ii) reduction of one ring of quinoxaline (**1**), and bromination of the tetrahydroquinoxalines with different reagents, solvents, and temperatures to access brominated quinoxalines, iii) synthesis of N-oxides of quinoxalines and bromination of them to obtain quinoxalines with bromine atoms in specific positions.

2.1 Bromination of quinoxaline (1) under different conditions

We first investigated the bromination of quinoxaline (**1**) under various conditions described in Table 1 and Scheme 2, and from this reaction the formation of different kinds of brominated product **9-14** was observed. Under the conditions in entries 5, 8, and 9, monobromide **10** was obtained exclusively in 51-65% yield. The reaction of **1** at 82 °C with 8 equiv. bromine in acetonitrile resulted in formation of only dibromide **12** in considerably high yield (entry 3). The photobromination reaction of **1** with molecular bromine (entry 7) gave us monobromide **9** in 70% yield as well as the dibromides **12** (10%) and **11** (3%). Synthesis of **9** starting from **1** using NBS in the presence of H_2SO_4 was first studied by Brown and Gouliaev[23] and they obtained **9** in only 12% yield. In the present work, thus, we have developed a good method for monobromide **9**. As is well known,[16,20] in the bromination reaction of hydrocarbons at high temperature, especially supported by photochemical conditions, the process proceeds via a radical intermediate. In some cases there is competition between the radical and the ionic reactions. In view of these points, we assumed that the reaction took place via addition of a bromine radical to a double bond, and elimination of the formed tetrabromide.[16,17,24] In other reaction conditions (entries 1, 2, 4, 6, 10, and 11) the formation of different product mixtures was observed. The reaction mixtures in that case were easily separated by column chromatography using SiO_2 with *n*-hexane/AcOEt. From this reaction, the dibromide **13** was synthesized in low yield. A better synthetic method was developed for dibromide **14**,[25] by photochemical bromination of **1** (entry 6) and bromination of **1** with molecular bromine in the presence of barium carbonate (entry 4) (Scheme 2).



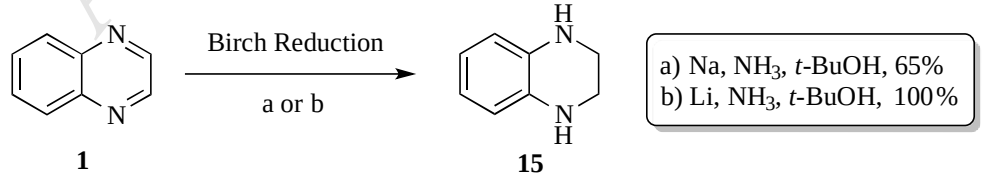
Scheme 2 Bromination of quinoxaline at different conditions

Entry	Method									
	Reagents	Solvent	T (°C)	Time, h	**9**	**10**	**11**	**12**	**13**	**14**
1	Br_2 (6.6 eq.)	CH_3CO_2H	Δ, 118	24	-	46	-	-	11	-
2	Br_2 (12 eq.)	H_2SO_4	Δ, 200	40	-	28	-	-	9	-
3	Br_2 (8 eq.)	CH_3CN	Δ, 82	25	-	-	-	**75**	-	-
4	Br_2 (8 eq.)/$BaCO_3$ (2 eq.)	CH_3CN	Δ, 82	25	-	31	14	5	6	28
5	Br_2 (3 eq.)/$BaCO_3$ (2 eq.)	CH_3CN	Δ, 82	72	-	**65**	-	-	-	-
6	Br_2 (8 eq.)	CCl_4	hν	18	-	-	-	30	-	25
7	Br_2 (2 eq.)	CCl_4	hν	45	**70**	-	3	10	-	-
8	NBS (6 eq.)/BPO	CH_3CO_2H	Δ, 118	20	-	**50**	-	-	-	-
9	NBS (6 eq.)/BPO	DMF	Δ, 153	18	-	**51**	-	-	-	-
10	NBS (7 eq.)/BPO	$CHCl_3$	Δ, 62	45	-	29	29	3	10	-
11	NBS (6 eq.)/BPO	CH_3CN	Δ, 82	20	-	55	15	-	5	-

Table 1: Bromination of quinoxaline (**1**) under different conditions with bromination agents. (BPO: Benzoyl peroxide, NBS: N-Bromosuccinimide, hv: A 150 W projector lamp).

2.2 Reduction of quinoxaline (1) and bromination of tetrahydroquinoxalines (15 and 19) under different conditions

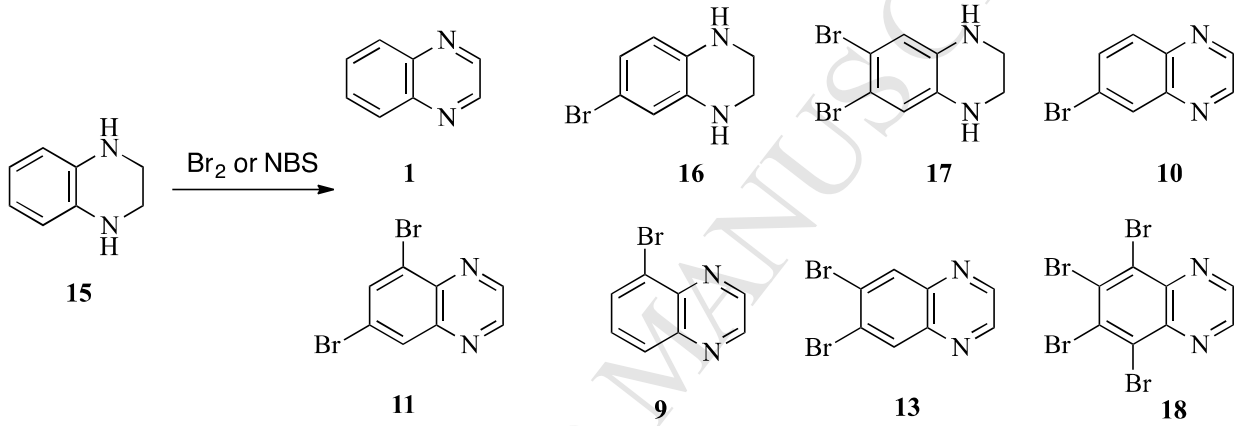
In our previous work we showed that bromination of saturated naphthalene, i.e. decalin, gave us a new kind of brominated naphthalene derivative in high yield.[16a] Similarly Cakmak and co-workers successfully brominated 1,2,3,4-tetrahydronaphthalene, tetralin.[17] Those methods encouraged us to study the bromination of reduced quinoxalines **15** and **19** under different reaction conditions. The compound **19** is commercially available, but isomeric **15** is expensive. Therefore, we first aimed to synthesize **15** starting from **1**. Many effective methods for reduction of quinoxaline **1** to **15** exist in the literature and few of them are patented.[26] In addition, although Birch reduction is one of the best methods for controlled reduction of aromatic rings, to the best of our knowledge, Birch reduction of **1** has not been reported in the literature. Reduction of **1** with metallic sodium in liquid ammonia gave the target compound **15** as the sole product in moderate yield (65%). Alternatively reduction of **1** was tried with metallic lithium, and compound **15** was obtained in excellent yield (100%) (Scheme 3). Thus, a new and effective method was developed for reduction of **1** to **15**.



1 **15**

Scheme 3 Synthesis of 1,2,3,4-tetrahydroquinoxaline

After the successful synthesis of **15**, this compound is prone to bromination under different reaction conditions, the results are reported in Scheme 4 and Table 2. As seen in Table 2, the bromination reaction of **15** with molecular bromine or NBS in chloroform or carbon tetrachloride results in only formation of aromatized compound **1** (entries 1-6). In addition, when the solvent was changed to acetonitrile, the bromination reaction of **15** with bromine gave brominated products **9**, **10**, **11**, **13**, **16**, **17**, and **18** as well as **1**. This method gave us the synthesis of monobromide **16**, dibromide **17**, and tetrabromide **18** in moderate yield. The first synthesis of tetrabromide **18** in up to 99% yield (entries 9-12) is particularly valuable for us as it may be a key compound for many kinds of functionalized quinoxaline derivatives for many applications.

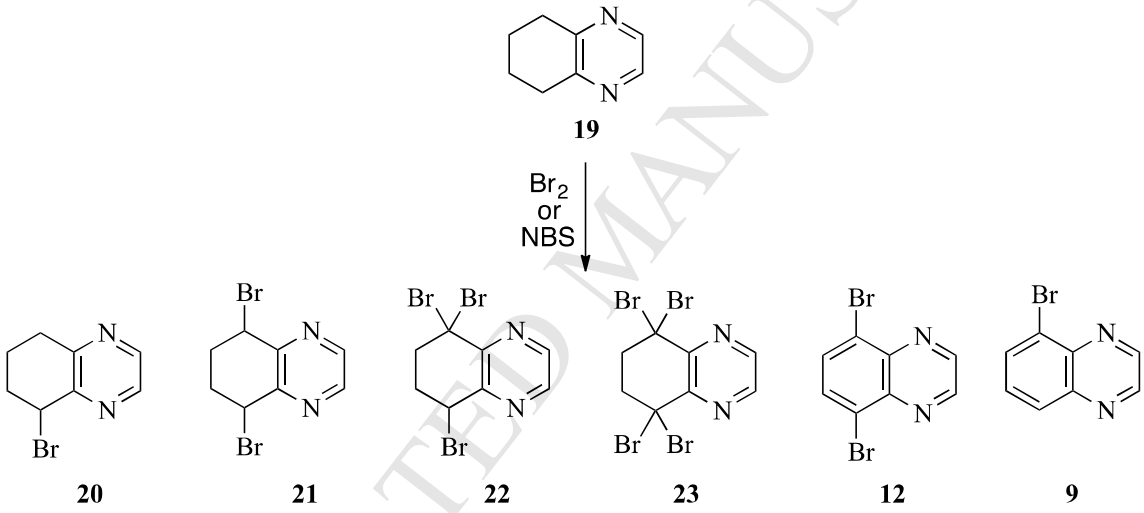


Scheme 4 Bromination of 1,2,3,4-tetrahydroquinoxaline at different conditions

Entry	Method				Compounds / Yield (%)							
	Reagent	Solvent	T (°C)	Time (h)	**1**	**16**	**17**	**10**	**13**	**9**	**11**	**18**
1	NBS (1 eq.)	$CHCl_3$	Δ, 62	2	35	-	-	-	-	-	-	-
2	NBS (1 eq.)	$CHCl_3$	hν, 62	2	35	-	-	-	-	-	-	-
3	Br_2 (1 eq.)	$CHCl_3$	Δ, 62	2	38	-	-	-	-	-	-	-
4	Br_2 (1 eq.)	$CHCl_3$	h, 62	2	30	-	-	-	-	-	-	-
5	Br_2 (2 eq.)	$CHCl_3$	Δ, 62	2	55	-	-	-	-	-	-	-
6	Br_2 (1 eq.)	CCl_4	hν	2	45	-	-	-	-	-	-	-
7	Br_2 (1 eq.)	CH_3CN	Δ, 82	2.5	50	30	20	-	-	-	-	-
8	Br_2 (2 eq.)	CH_3CN	Δ, 82	2.5	35	15	10	7	5	-	5	-
9	Br_2 (6 eq.)	CH_3CN	Δ, 82	2.5	35	-	-	11	6	4	5	17
10	Br_2 (6 eq.)	CH_3CN	Δ, 82	10	50	-	-	-	-	-	-	50
11	Br_2 (12 eq.)	CH_2Cl_2	25	15	-	-	-	-	25	-	-	65
12	Br_2 (30 eq.)	-	4, dark	48	-	-	-	-	-	-	-	**99**

Table 2: Bromination of 1,2,3,4-tetrahydroquinoxaline (**15**) at different condition with bromination agents. (BPO: Benzoyl peroxide, NBS: N-Bromosuccinimide, hv: A 150 W projector lamp).

The bromination reaction of isomeric tetrahydroquinoxaline **19** with molecular bromine was also studied and the results are reported in Table 3 and Scheme 5. Depending on the reaction conditions, such as solvent, reagent, temperature, light, and quantities of bromination agents, the formation of different kinds of bromination product was observed. The reaction of **19** with 1.0 equiv. bromine at 82 °C (entry 1) in acetonitrile gave monobromide **20**[27] in 82% yield. When we used 2.0 equiv. bromine (entry 3) the formation of dibromide **21** was observed as a major product in 86% yield. We showed that tetrabromide **23** was formed as the sole product in nearly quantitative yield by the bromination reaction of **19** with 6.0 equiv. bromine at 82 °C in acetonitrile (entry 7). When 3.0 equiv. bromine was used, tribromide **22** was obtained in high yield (85%). These experiments are valuable for us because tribromide **22** and tetrabromide **23** are starting compounds for the monobromide **9** and the dibromide **12**, respectively, as shown in Scheme 6.



Scheme 5 Bromination of 5,6,7,8-tetrahydroquinoxaline at different conditions

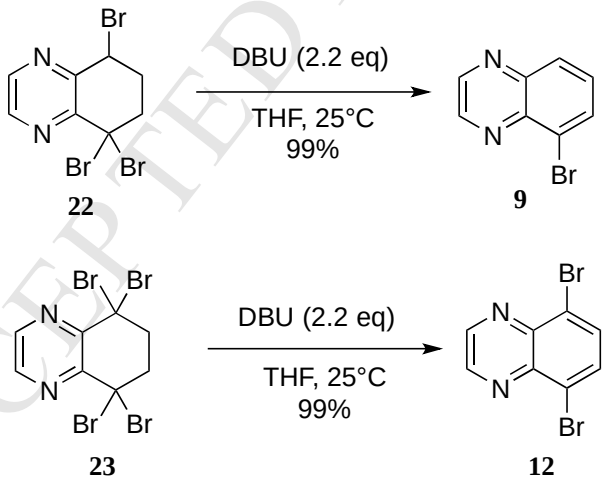
Entry	Method				Compounds / Yield (%)					
	Reagent	Solvent	T (°C)	Time	20	21	22	23	12	9
1	Br_2 (1 eq.)	CH_3CN	Δ, 82	2	**82**	9	-	-	-	-
2	Br_2 (1 eq.)	$CHCl_3$	Δ, 62	2	55	7	-	-	-	-
3	Br_2 (2 eq.)	CH_3CN	Δ, 82	2	10	**86**	4	-	-	-
4	Br_2 (2 eq.)	$CHCl_3$	Δ, 62	2	5	70	-	-	-	-
5	Br_2 (3 eq.)	CH_3CN	Δ, 82	2.5	-	8	**85**	5	-	2
6	Br_2 (3 eq.)	$CHCl_3$	Δ, 62	2.5	-	15	60	5	-	-
7	Br_2 (6 eq.)	CH_3CN	Δ, 82	3	-	-	-	**99**	-	-
8	Br_2 (6 eq.)	$CHCl_3$	Δ, 62	3	-	-	10	75	-	-
9	Br_2 (1.1 eq.)	CCl_4	hν	0.5	70	15	-	-	-	-
10	Br_2 (2.1 eq.)	CCl_4	hν	0.5	-	85	-	-	-	12
11	Br_2 (3.1 eq.)	CCl_4	hν	0.75	-	14	43	-	-	24
12	Br_2 (4.1 eq.)	CCl_4	hν	0.75	-	-	-	53	32	5

13	NBS (6 eq.)/BPO	CH_3CN	Δ, 82	2	35	55	-	-	-	-
14	NBS (6 eq.)/BPO	$CHCl_3$	Δ, 62	2	20	40	-	-	-	-
15	NBS (6 eq.)/BPO	CCl_4	hν	2	18	42	-	-	-	-

Table 3: Bromination of 5,6,7,8-tetrahydroquinoxaline (**19**) under different conditions with bromination agents. (BPO: Benzoyl peroxide, NBS: N-Bromosuccinimide, hv: A 150 W projector lamp).

Unlike isomer **15**, which gave mainly aromatic compounds during bromination reactions, it is noteworthy that bromination of **19** mostly results in the formation of saturated bromine functionalized products as described in Scheme 5 and Table 3. This showed that the nitrogen-containing ring is easily oxidized under the reaction conditions, while the other ring is more stable under those conditions. This assumption was proved during the aromatization reaction of this kind of product with DDQ, and we observed that while the nitrogen ring is easily aromatized with DDQ, the other ring shows resistance to the oxidation reaction. For example, the aromatization reaction of saturated compound **20** and **21** with DDQ under mild conditions does not work.

As saturated compounds **22** and **23** are formed in high yield (entries 5 and 7 in Table 3), these compounds were treated with base and alternative and effective synthetic protocols were developed for monobromide **9** and dibromide **12** in nearly quantitative yield (Scheme 6).

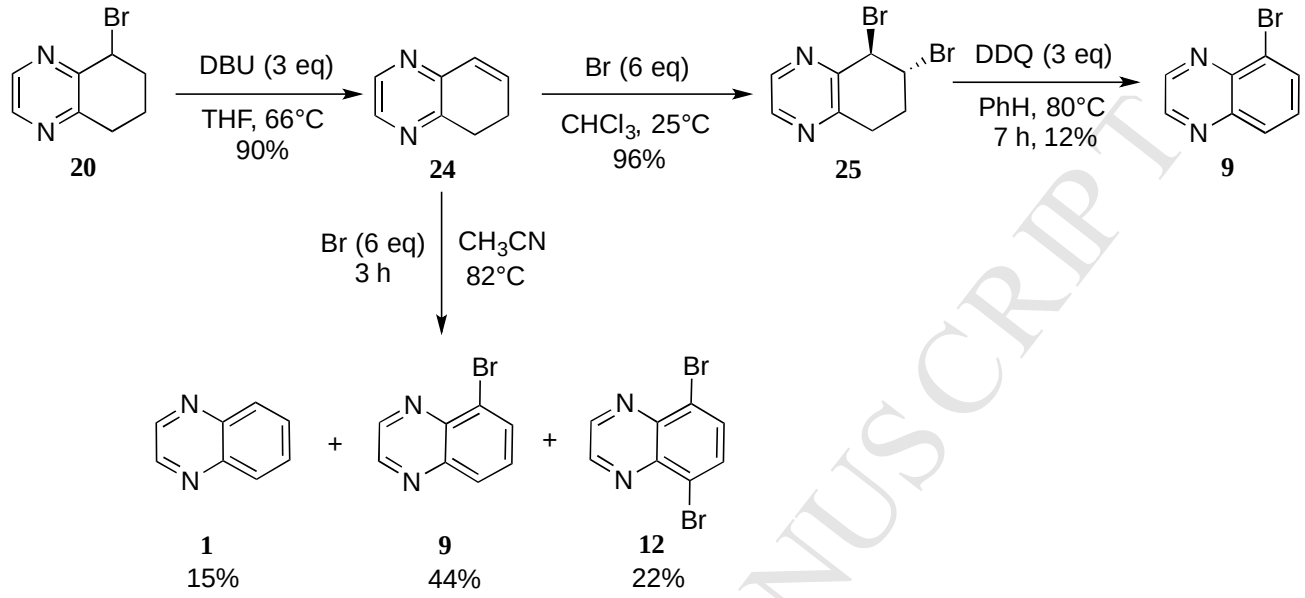


22 **9** **23** **12**

Scheme 6 Synthesis of brominated quinoxalines by elimination reaction

Furthermore, the reaction of monobromide **20**, formed in 82% yield (entry 1, in Table 3), was also studied to access brominated quinoxalines to discover effective or alternative methods. For this purpose, monobromide **20** was converted to alkene **24** by a base supported elimination reaction. Addition of bromine to **24** gave *trans* dibromide **25**. The aromatization reaction of **25** with DDQ resulted in the formation of **9**. Bromination of **24** with excess bromine at 82 °C gave monobromide **9**, dibromide **12**,

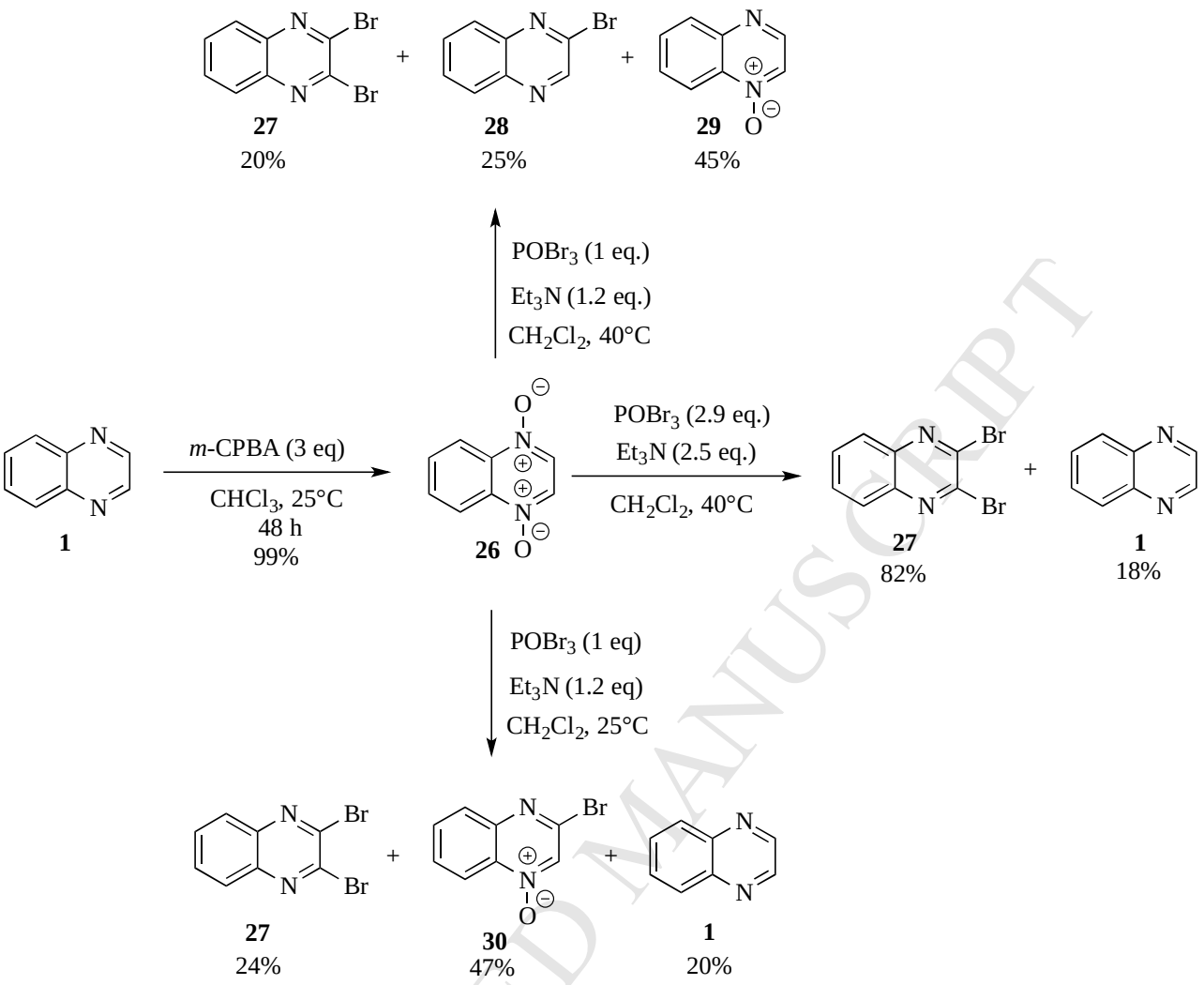
and parent compound quinoxaline **1** in 44%, 22%, and 15% yield, respectively (Scheme 7).



Scheme 7 Synthesis of brominated quinoxalines

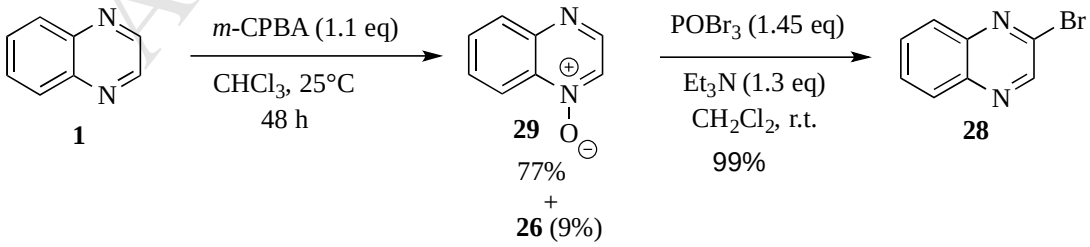
2.3 Synthesis of N-oxides of quinoxalines and bromination of N-oxides

As shown in Schemes 2, 4, and 5, the direct bromination of quinoxaline (**1**) and saturated derivatives **15** and **19** gave only products derived on the benzene ring due to electron deficiency in the heterocyclic ring. For derivatives on the heterocyclic ring, we also studied the bromination of N-oxide derivatives, as oxygen atoms increase the electron density of the heterocyclic ring by a resonance effect. For this purpose, quinoxaline (**1**) was oxidized to bis N-oxide **26**[28] by *meta*-chloroperbenzoic acid (*m*-CPBA) in nearly quantitative yield. Bromination of **26** with $POBr_3$ (2.9 eq.) in the presence of NEt_3 in methylene chloride at 40 °C gave the target compound dibromide **27**[29] in 82% yield as well as deoxygenated compound **1** in 18% yield. Under the same reaction conditions, when we used $POBr_3$ in lower quantity (1.0 eq.), we obtained monobromide **28** in 25% yield along with dibromide **27** (20%) and mono N-oxide **29**[30] (45%). We also noticed that the reaction temperature has a dramatic effect on product distribution. Reaction at 25 °C produced monobromo N-oxide **30** as the major product as well as dibromide **27** and deoxygenated compound **1** in 20% and 24% yields, respectively.



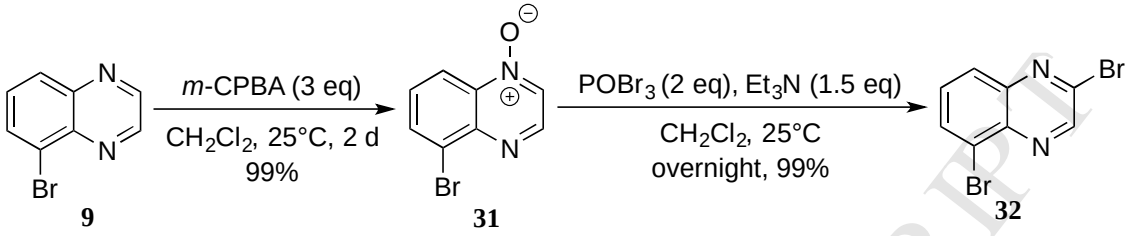
Scheme 8 Synthesis of brominated quinoxalines via its N-oxide derivatives

After the successful synthesis of the dibromide **27**, we turned our attention towards the synthesis of monobromide **28**[31] via mono N-oxide **29**[29] obtained by the reaction of **1** with *m*-CPBA (1.1 eq.) in 77% yield in addition to bis N-oxide **26** (9%). From the reaction of N-oxide **26** with $POBr_3$ (1.45 eq.), target compound **28**[31] was successfully obtained in 99% yield (Scheme 9).



Scheme 9 Synthesis of 2-bromoquinoxaline via its N-oxide derivative

Similar transformation of compound **9** to compound **32** was accomplished via N-oxide **31** in nearly quantitative yield (Scheme 10). This reaction allowed the first and effective synthesis of the dibromide **32**.



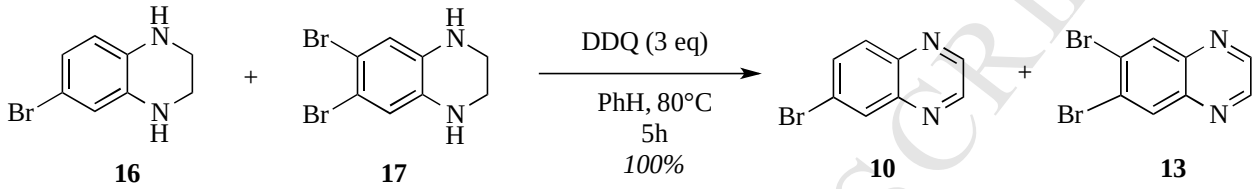
Scheme 10 Synthesis of 2,6-dibromoquinoxaline via its N-oxide derivative

2.4 Structural analyses

The structures of these compounds were elucidated on the basis of ^{1}H- and ^{13}C-NMR spectral data and elemental analyses, and by comparison of some spectral data of related systems reported in the literature. The position of substituents in quinoxaline units is easily determined by vicinal and allylic coupling constants. As compounds **12** and **13** are symmetrical in structure, it is not easy to determine which one is which as both of them give two singlets in the ^{1}H-NMR and four lines in the ^{13}C-NMR spectra. As physical data for compound **12** exists in the literature,[22] it is easy to identify this compound by means of its physical and spectral data. It is clear that the other compound should be structure **13**. In addition, H_5 and H_8 protons in compound **13** resonate at a higher field than H_6 and H_7 protons of dibromide **12**. These confirm the assigned structure. The other symmetric dibromide **27** also has four lines in the ^{13}C-NMR spectrum due to its symmetrical structure. Unlike the other symmetric dibromides **12** and **13**, the typical AA'BB' system of the benzene ring in the ^{1}H-NMR spectra exactly confirms the structure of dibromide **27**. Only one singlet in the ^{1}H-NMR spectrum and four lines in the ^{13}C-NMR spectrum confirm the structure of tetrabromide **18** by assistance from elemental analyses.

It is not easy to find the exact configuration of substituents in compound **21** because of its symmetrical structure and highly complex second order spin system in the ^{1}H-NMR spectra. However, we assumed that the substituents should be trans in this compound, as bulky groups should be in equatorial-equatorial orientations, which are typical for 1,2-, and 1,4- substituted cyclohexane and cyclohexene rings, which are sterically more favorable.

Because of the similar Rf values and solubility in solvents, monobromide **16** and dibromide **17** could not be isolated as pure compounds. However, NMR analysis of a mixture provided us with enough information for assignment of all signals of the proposed structures. For further support of the structures, the mixture of these compounds was subjected to oxidation with DDQ. Monobromide **10** and dibromide **13** were obtained in quantitative yield, and this mixture could be easily separated by a combination of sublimation and column chromatography. This transformation both supports the proposed structures and also allows an alternative synthesis of monobromide **10** and dibromide **13** (Scheme 14).



16 + **17** → **10** + **13**

Scheme 14 Aromatization of saturated quinoxalines

3. Conclusion

We have described an efficient and convenient synthesis of brominated quinoxalines. We showed that bromination of a parent compound under different conditions results in the formation of several new compounds in high yield along with the known derivatives. The bromination reaction of tetrahydroquinoxaline generally produced aromatization of the ring and formed parent compound **1** along with a few halogenated compounds, whereas bromination of isomeric tetrahydroquinoxaline gave a bromination product over the saturated ring. Bromination of N-oxides gave us a brominated product on the ring with nitrogen atoms. An alternative and effective synthetic method is developed also for reduction of quinoxaline to tetrahydroquinoxaline. These compounds are potential starting points for polyfunctionalization to quinoxaline derivatives that are important for many applications such as materials chemistry or for synthesis of biomaterials. Some transformation and functionalization reactions of this compound are in progress.

4. Experimental

4.1 General remarks

All reactions were carried out under nitrogen and monitored by TLC and/or ^{1}H-NMR spectroscopy. All solvents were dried and distilled before use. Column chromatography was performed on silica gel (60 mesh, Merck). TLC was carried out on Merck 0.2 mm silica gel 60 F254 anal. aluminum plates. Melting points are uncorrected. The ^{1}H- and ^{13}C-NMR spectra were recorded on 400 MHz NMR

spectrometers. Apparent splittings are given in all cases in ppm and coupling constants *J* in Hz. All new compounds gave satisfactory HRMS or elemental analyses.

4.1.1 General methods for high temperature bromination of quinoxaline and derivatives

Bromine was added dropwise to a magnetically stirred refluxing solution of quinoxaline (**1**) or tetrahydroquinoxaline **15** or **19** in the relevant solvent. The resulting reaction mixture was heated at reflux temperature. The reaction was monitored by TLC or ^{1}H-NMR spectroscopy. After the desired time, the resulting reaction mixture was allowed to cool to room temperature and the solvent was removed under reduced pressure. The mixture was diluted with a saturated solution of sodium carbonate (10 mL) and the mixture was extracted with ethyl acetate (2x25 mL). Combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The crude was purified appropriate method described in below.

4.1.2 General methods for photochemical bromination of quinoxaline and derivatives

A solution of quinoxaline (**1**) or tetrahydroquinoxaline **15** or **19** in CCl_4 (10 mL) was irradiated with a 500-W lamp in a 25-mL flask equipped with a reflux condenser. Bromine was added dropwise to the refluxing solution and the solution was irradiated at reflux temperature. The reaction was monitored by TLC or ^{1}H-NMR spectroscopy. The resulting reaction mixture was allowed to warm to room temperature and diluted with a saturated solution of sodium carbonate (10 mL). The mixture was extracted with methylene chloride (2x25 mL) and the combined organic layers were washed with water, dried over Na_2SO_4 and concentrated.

4.2 Bromination of Quinoxaline (1) with Bromine in AcOH

The reaction was carried out by the general procedure described in section 4.1.1 using quinoxaline (**1**) (390 mg, 3.0 mmol), bromine (3.16 g, 19.8 mmol) and glacial acetic acid (10 mL). The resulting reaction mixture was kept at reflux temperature for 24 h.

6,7-Dibromoquinoxaline (**13**) was separated by crystallization from methanol (400 mg, 46%). White solid, mp 200-202 °C (lit[20e] mp= 210-212 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 2H), 8.45 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 142.2, 133.6, 126.9. IR (KBr, cm^{-1}): 3061*s*, 3036*s*, 2964*m*, 1575*w*, 1454*w*, 1421*w*, 1329*w*, 1184*m*, 915*s*. MS (EI, 70 eV): m/z 291/289/287(M^+, 100), 236/234 (25),

210/208 (M^+ -Br, 50), 155 (5). Anal. Calcd. for $C_8H_4Br_2N_2$: C, 33.37, H, 1.40, N, 9.73%. Found: C, 33.41, H, 1.42, N, 9.58.

6-Bromoquinoxaline (**10**)[20] was obtained by sublimating of the remaining part of residue at 125 °C (70 mg, 11%). White solid, mp 49-51 °C (lit[20f] mp= 48-49 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88-8.84 (m, 2H), 8.31 (d, *J* = 2.0 Hz, 1H), 7.99 (d, *J* = 8.9 Hz, 1H), 7.87 (dd, *J* = 8.9 and 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 145.2, 143.6, 141.8, 133.7, 131.8, 130.9, 124.1. IR (KBr, cm^{-1}) 3059*w*, 1592*w*, 1482*s*, 1356*m*, 1204*m*, 1170*m*, 1127*m*, 1020*s*, 822*s*. MS (EI, 70 eV): m/z 210/209(M+, 100), 156(15), 130(M+ -Br, 10). Anal. Calcd. for $C_8H_5BrN_2$: C, 45.97, H, 2.41, N, 13.40%. Found: C, 45.45, H, 2.29, N, 13.35.

4.3 Bromination of Quinoxaline (1) with Bromine in Sulfuric Acid

The reaction was carried out by the general procedure described in section 4.1.1 using quinoxaline (**1**) (390 mg, 3.0 mmol), bromine (2.43 g, 15.2 mmol) and sulfuric acid (10 mL). The resulting reaction mixture was kept at 200 °C for 24 h.

6,7-Dibromoquinoxaline (**13**) (80 mg, 9%) data as above.

6-Bromoquinoxaline (**10**) (175 mg, 28%). data as above

4.4 Bromination of Quinoxaline (1) with Bromine in Acetonitrile

The reaction was carried by the general procedure described in section 4.1.1 using quinoxaline (**1**) (390 mg, 3.0 mmol), bromine (3.84 g, 24.0 mmol) and acetonitrile (20 mL). The resulting reaction mixture was kept at reflux temperature for 25 h. The residue was purified via column chromatography on silica gel (30 g) by eluting with 15% EtOAc/*n*-hexane. 5,8-Dibromoquinoxaline (**12**) was obtained as a sole product.

5,8-Dibromoquinoxaline (**12**)[22] (650 mg, 75%). Brown solid, decom. 225 °C (lit[22d] mp= 229 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 2H), 8.00 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 141.6,

133.7, 124.0. IR (KBr, cm^{-1}) 3048*w*, 1449*m*, 1374*m*, 1170*m*, 1110*w*, 1025*w*, 972*s*. Anal. Calcd. for $C_8H_4Br_2N_2$: C, 33.37, H, 1.40, N, 9.73%. Found: C, 33.42, H, 1.54 , N, 9.66.

4.5 Bromination of Quinoxaline (1) with Bromine (8 eq) in CCl_4

The reaction was carried out by the general procedure described in section 4.1.2 using quinoxaline (**1**) (390 mg, 3.0 mmol), bromine (3.84 g, 24.0 mmol) and carbon tetrachloride (20 mL). The resulting reaction mixture was kept at reflux temperature for 18 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromoquinoxaline (**12**) (260 mg, 30%) data as before.

The second fraction was 5,6-dibromoquinoxaline (**14**)[25] (215 mg, 25%). White solid, mp 182-184°C (lit[25] mp 182-184.3 °C, decomposition). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98-8.95 (m, 1H), 8.90-8.88 (m, 1H), 8.00-7.97 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 145.4, 142.6, 142.0, 134.5, 129.7, 128.1, 127.1. IR (KBr, cm^{-1}): 3012*m*, 1589*w*, 1471*m*, 1396*m*, 1351*m*, 1112*s*, 1030*s*, 966*s*. Anal. Calcd. for $C_8H_4Br_2N_2$: C, 33.37, H, 1.40, N, 9.73%. Found: C, 33.66, H, 1.65, N, 9.79.

4.6 Bromination of Quinoxaline (1) with Bromine (2 eq) in CCl_4

The reaction was carried out by the general procedure described in section 4.1.2 using quinoxaline (**1**) (390 mg, 3.0 mmol), bromine (960 mg, 6.0 mmol) and carbon tetrachloride (15 mL). The resulting reaction mixture was kept at reflux temperature for 45 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5-bromoquinoxaline (**9**)[19] (440 mg, 70%). White solid, mp 68-69 °C (lit[19b] mp 65-67 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97-8.95 (m, 1H), 8.89-8.87 (m, 1H), 8.10 (bd, J=8.0 Hz, 1H), 8.09 (dd, J=8.0 Hz, *J* = 2.3 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 145.4, 144.0 140.7, 133.6, 130.3, 129.5, 124.1. IR (KBr, cm^{-1}): 3060*w*, 1601*w*, 1554*w*, 1485*m*, 1458*w*, 1057*m*, 1025*m*, 967*s*, 767*s*. MS (EI, 70 eV): m/z /210/208(M^+, 60), 181 (20), 156 (20), 130 (M^+ -Br, 15), 102 (20), 75 (100). Anal. Calcd. for $C_8H_5BrN_2$: C, 45.97, H, 2.41, N, 13.40%. Found: C, 46.36, H, 2.65, N, 12.92.

The second fraction was 5,8-dibromoquinoxaline (**12**) (85 mg, 10%) data as before.

The third fraction was 5,7-dibromoquinoxaline (**11**)[21] (25 mg, 3%). White solid, mp 162-164 °C (lit[21] mp, it is not given). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, A-part of AB system, J = 1.7 Hz, 1H), 8.88 (d, B-part of AB system, J = 1.7 Hz, 1H), 8.29 (d, A-part of AB system, J = 2.0 Hz, 1H), 8.22 (d, B-part of AB system, J = 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 145.6, 144.1, 139.7, 136.6, 131.7, 125.2, 123,8. IR (KBr, cm^{-1}): 3064*w*, 3048*w*, 3036*w*, 2917*w*, 1634*b*, 1548*w*, 1466*w*, 1363*w*, 1095*b*, 1031*w*, 967*w*, 883*m*. Anal. Calcd. for $C_8H_4Br_2N_2$: C, 33.37, H, 1.40, N, 9.73%. Found: C, 33.69, H, 1.51, N, 9.82.

4.7 Bromination of Quinoxaline (1) with NBS in AcOH or DMF

A solution of quinoxaline (**1**) (390 mg, 3.0 mmol), NBS (390 mg, 3.0 mmol), and benzoyl peroxide (catalytic amount) in glacial acetic acid (10 mL) was heated at reflux temperature for 20h. The reaction was monitored by TLC or ^{1}H-NMR spectroscopy. The resulting reaction mixture was allowed to cool to room temperature and the solvent was removed under reduced pressure. The mixture was diluted with a saturated solution of sodium carbonate (10 mL) and the mixture was extracted with ethyl acetate (2x25 mL). Combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. 6-Bromoquinoxaline (**10**) (315 mg, 50%) was obtained as a sole product. The reaction was repeated using DMF as a solvent at the same reaction condition and monobromide **10** was obtained in 51% yield.

4.8 Bromination of Quinoxaline with NBS in $CHCl_3$

The reaction was carried out by the procedure described in section 4.7 using quinoxaline (**1**) (390 mg, 3.0 mmol), NBS (3.74 g, 21.0 mmol) and chloroform (20 mL). The resulting reaction mixture was kept at reflux temperature for 45 h. The residue was purified via column chromatography on silica gel (100 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 6-bromoquinoxaline (**10**) (180 mg, 29%) data as before.

The second fraction was 5,8-dibromoquinoxaline (**12**) (25 mg, 3%) data as before.

The third fraction was 6,7-dibromoquinoxaline (**13**) (85 mg, 10%) data as before.

The fourth fraction was 5,7-dibromoquinoxaline (**11**) (250 mg, 29%) data as before.

4.9 Bromination of Quinoxaline (1) with NBS in CH_3CN

The reaction was carried out by the procedure described in section 4.7 using quinoxaline (**1**) (390 mg, 3.0 mmol), NBS (3.20 g, 18.0 mmol) and acetonitrile (20 mL). The resulting reaction mixture was kept at reflux temperature for 20 h. The residue was purified via column chromatography on silica gel (100 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 6-bromoquinoxaline (**10**) (345 mg, 55%) data as before.

The second fraction was 5,8-dibromoquinoxaline (**12**) (45 mg, 5%) data as before.

The third fraction was 6,7-dibromoquinoxaline (**13**) (130 mg, 15%) data as before.

4.10 Bromination of Quinoxaline (1) with Bromine (8 eq) and Barium Carbonate

Bromine (3.84 g, 24 mmol) was added dropwise to a magnetically stirred refluxing mixture of quinoxaline (**1**) (390 mg, 3.0 mmol) and barium carbonate (1.20 g, 6.1 mmol) in acetonitrile (20 mL). The resulting reaction mixture was heated at reflux temperature for 25 h and allowed to warm to room temperature. The solvent was evaporated and the mixture was diluted with a saturated solution of sodium carbonate (10 mL). The mixture was extracted with ethyl acetate (3x25 mL) and combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (100 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 6-bromoquinoxaline (**10**) (195 mg, 31%) data as before.

The second fraction was 5,8-dibromoquinoxaline (**12**) (45 mg, 5%) data as before.

The third fraction was 6,7-dibromoquinoxaline (**13**) (50 mg, 6%) data as before.

The fourth fraction was 5,7-dibromoquinoxaline (**11**) (120 mg, 14%) data as before.

The fifth fraction was 5,6-dibromoquinoxaline (**14**) (240 mg, 28%) data as before.

4.11 Bromination of Quinoxaline (1) with Bromine (3 eq) and Barium Carbonate

Bromine (1.44 g, 9.0 mmol) was added (partly as three portions in 48h) to a magnetically stirred refluxing mixture of quinoxaline (**1**) (390 mg, 3.0 mmol) and barium carbonate (1.20 g, 6.1 mmol) in acetonitrile (20 mL) at reflux temperature. The resulting reaction mixture was heated at reflux temperature for 72h and allowed to cool to room temperature. The solvent was evaporated and the mixture was diluted with saturated solution of sodium carbonate (10 mL). The mixture was extracted with ethyl acetate (3x25 mL) and combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (20 g) by eluting with 15% EtOAc/*n*-hexane and 6-bromoquinoxaline (**10**) (410 mg, 65%) was obtained.

4.12 Birch reduction of quinoxaline (1) with sodium in ammonia:

A two-necked round-bottomed flask (1 L) was immersed in an acetone–dry ice bath and fitted with a dry ice condenser. Ammonia (100 mL) was condensed into the flask at -78 °C and sodium (4.60 g, 200.0 mmol) was added in small portions, with vigorous stirring, over a period of 15 min. The mixture was stirred at -40 °C for 30 min. and a solution of quinoxaline (**1**) (2.60, 20 mmol) in THF (20 mL) was added dropwise to the blue solution at -78 °C over 15 min. The reaction mixture was stirred at -78 °C for 1 hour and *t*-butyl alcohol (14.82 g, 200.0 mmol) was added dropwise to the reaction mixture. After the addition was complete, the reaction mixture was stirred at -78 °C for another 1 hour. The cooling bath was removed and the ammonia was allowed to evaporate overnight. A solution of ammonium chloride (20 mL) was added to the mixture and the mixture was extracted with ethyl acetate (3x50 mL). Combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (100 g) by eluting with 10% EtOAc/*n*-hexane and 1,2,3,4-tetrahydroquinoxaline **15**[26] was obtained as a brown solid (1.75 g, 65%, mp 91-93 °C (lit[26j] mp 95.5-97 °C)).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 (AA' part of AA'BB' system, 2H), 6.50 (BB' part of AA'BB' system, 2H), 3.42 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.6, 118.7, 114.6, 41.3. IR (KBr, cm^{-1}): 3245*s*, 3048*w*, 2980*m*, 2922*m*, 1600*m*, 1506*m*, 1356*w*, 1309*w*, 1270*w*, 1242*w*, 1104*w*, 1049*w*, 735*s*. (EI, 70 eV): m/z 136/135 (M^+, 100). Anal. Calcd. for $C_8H_{10}N_2$: C, 71.61, H, 7.51, N, 20.88%. Found: C, 71.47, H, 7.73, N, 20.61.

4.13 Birch reduction of quinoxaline (1) with lithium in ammonia:

Lithium (2.64 g, 380.0 mmol) was added to a magnetically stirred solution of quinoxaline (**1**) (2.6 g, 20.0 mmol) in dry ether at 0°C under Ar atm over 15 min. *t*-Butyl alcohol (20.16 g, 272.0 mmol) was added slowly to the reaction mixture and the mixture was stirred at 0°C under ammonia atm for 7 h and overnight at room temperature. A solution of ammonium chloride (30 mL) was added to the mixture and the mixture was extracted with ether (3x50 mL). Combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (100 g) by eluting with 10% EtOAc/*n*-hexane and tetrahydroquinoxaline **15** was obtained as a brown solid (2.65 g, 99%).

4.14 Bromination of Tetrahydroquinoxaline 15 with Bromine (1 eq):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **15** (270 mg, 2.0 mmol), bromine (350 mg, 2.2 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 2.5 h. Quinoxaline was purified via column chromatography on silica gel (50 g) by eluting with 20% EtOAc/*n*-hexane.

Quinoxaline (**1**): 130 mg, 50% data as before.

6-Bromo-1,2,3,4-tetrahydroquinoxaline (**16**),[26g] (130 mg, 30%) was isolated as a mixture with **17** in a ratio of (3:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (dd, J = 8.2 Hz and J = 2.1 Hz, 1H), 6.58 (d, J = 2.1 Hz, 1H), 6.34 (d, J = 8.2 Hz, 1H), 3.61 (bs, 2H), 3.38 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.0, 132.5, 120.8, 116.6, 115.5, 110.1, 41.0 (2C).

6,7-Dibromo-1,2,3,4-tetrahydroquinoxaline (**17**): 120 mg, 20%

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (s, 2H), 3.61 (bs, 2H), 3.36 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.0, 117.7, 111.3, 40.7.

4.15 Bromination of Tetrahydroquinoxaline 15 with Bromine (2 eq):

The reaction was carried by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **15** (270 mg, 2.0 mmol), bromine (675 mg, 4.2 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 2.5 h. The solvent was removed, and then methanol was added to the mixture, the insoluble dibromide **11** (30 mg, 5%) was collected by filtration. The residue was filtered via column including silica gel and products were analyzed by ^{1}H-NMR spectroscopy.

Quinoxaline (**1**): 92 mg, 35% data as before.

6-Bromo-1,2,3,4-tetrahydroquinoxaline (**16**): 65 mg, 15% data as before.

6,7-Dibromo-1,2,3,4-tetrahydroquinoxaline (**17**): 60 mg, 10% data as before.

6-Bromoquinoxaline (**10**): 30 mg, 7% data as before.

6,7-Dibromoquinoxaline (**13**): 30 mg, 5% data as before.

4.16 Bromination of Tetrahydroquinoxaline 15 with Bromine (6 eq):

The reaction was carried by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **15** (270 mg, 2.0 mmol), bromine (2.0 g, 12.5 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 2.5 h. The residue was filtered via column including silica gel and products were analyzed by ^{1}H-NMR spectroscopy.

Quinoxaline (**1**): 92 mg, 35% data as before.

6-Bromoquinoxaline (**10**): 48 mg, 11% data as before.

6,7-Dibromoquinoxaline (**13**): 35 mg, 6% data as before.

5-Bromoquinoxaline (**9**): 15 mg, 4% data as before.

5,7-Dibromoquinoxaline (**11**): 30 mg, 5% data as before.

5,6,7,8-Tetrabromoquinoxaline (**18**): 150 mg, 17%, brown solid, mp >300 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 140.4, 136.9, 125.6. IR (KBr, cm^{-1}): 3031*w*, 1687*w*,1425*w*, 1333*w*, 1030*w*, 983*w*. Anal. Calcd. for $C_8H_2Br_4N_2$: C, 21.56, H, 0.45, N, 6.28%. Found: C, 22.03, H, 0.67, N, 6.10.

4.17 Bromination of Tetrahydroquinoxaline 15 with Bromine (6 eq):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **15** (135 mg, 1.0 mmol), bromine (1.0 g, 6.3 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 10 h. 5,6,7,8-tetrabromoquinoxaline (**18**) (225 mg, 50%) was separated by crystallization from ethyl acetate.

Quinoxaline (**1**): 65 mg, 50%.

4.18 Bromination of Tetrahydroquinoxaline 15 with Bromine (12 eq):

Bromine (1.0 g, 6.3 mmol) was added dropwise to a magnetically stirred solution of tetrahydroquinoxaline **15** (135 mg, 1.0 mmol) in methylene chloride at room temperature. The resulting reaction mixture was stirred for 15 h. The mixture was diluted with a saturated solution of sodium carbonate (10 mL) and the mixture was extracted with methylene chloride (3x25 mL). The combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. Methanol was added to the mixture, the insoluble tetrabromide **18** (290 mg, 65%) was collected by filtration. Methanol was removed, and then the residue was recrystallized from methylene chloride and 6,7-dibromoquinoxaline (**13**) (72 mg, 25%) was obtained.

4.19 Bromination of Tetrahydroquinoxaline 15 with Bromine (30 eq):

A mixture of 1,2,3,4-tetrahydroquinoxaline (**15**) (135 mg, 1.0 mmol) and bromine (4.82 g, 30.2 mmol) was stirred in dark at 4 °C for 4 day. After bromine was removed, 5,6,7,8-tetrabromoquinoxaline (**18**) (445 mg, 99%) was obtained in quantitative yield.

4.20 Bromination of Tetrahydroquinoxaline 19 with Bromine (1 eq):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (350 mg, 2.2 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 2 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (55 mg, 9%), white solid, decom.>130°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 2H), 5.58 (bd, J = 2.9 Hz, 2H), 2.87 (bd, A-part of AB system, J = 10.6 Hz, 2H), 2.46 (bd, B-part of AB system, J = 10.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 144.7, 48.7, 28.1. IR (KBr, cm^{-1}): 3047*w*, 2964*m*, 2912*w*, 2846*w*, 1434*s*, 1407*s*, 1341*w*, 1233*w*, 1199*s*, 1175*m*, 1085*w*, 1047*m*, 1007*m*, 932*s*. MS (EI, 70 eV): m/z 291/290/289 (M^+, 5), 213/212 (M^+ -Br, 10), 131 (M^+ -2Br, 100). Anal. Calcd. for $C_8H_8Br_2N_2$: C, 32.91, H, 2.76, N, 9.59%. Found: C, 33.40, H, 2.95, N, 9.47.

The second fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**)[27] (350 mg, 82%), brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44-8.40 (m, 2H), 5.52-5.49 (m, 1H), 3.21-310 (m, 1H), 3.09-2.96 (m, 1H), 2.53-2.44 (m, 1H), 2.41-2.22 (m, 2H), 2.09-2.00 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 151.3, 143.9, 142.4, 50.1, 32.4, 31.1, 18,2. IR (KBr, cm^{-1}): 3046*w*, 2949*m*, 2874*w*, 1646*b*, 1456*m*, 1428*m*, 1403*s*, 1194*m*, 1182*m*, 1169*m*, 1143*m*, 1080*w*, 1054*m*, 1042*m*, 934*m*. MS (EI, 70 eV): m/z 214/212 (M^+, 10), 168(4), 134(M^+ -Br, 100). Anal. Calcd. for $C_8H_9BrN_2$: C, 45.10, H, 4.26, N, 13.15%. Found: C, 45.41 , H, 4.25, N,12.91.

4.21 Bromination of Tetrahydroquinoxaline 19 with Bromine (1 eq.):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (350 mg, 2.2 mmol) and chloroform (10 mL). The resulting reaction mixture was kept at reflux temperature for 2h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (42 mg, 7%) data as before.

The second fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**) (235 mg, 55%) data as before.

4.22 Bromination of Tetrahydroquinoxaline 19 with Bromine (2 eq.):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (650 mg, 4.1 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 2 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,5,8-tribromo-5,6,7,8-tetrahydroquinoxaline (**22**) (30 mg, 4%), white solid, decom. > 75 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.55 (s, 1H), 5.51-5.47 (m, 1H), 3.62-3.50 (m, 1H), 3.27-3.18 (m, 1H), 2.80-2.68 (m, 1H), 2.43-2.34 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 146.4, 145.7, 145.2, 61.4, 47.7, 43.8, 30.9. IR (KBr, cm^{-1}): 3044*w*, 2965*w*, 2923*w*, 2848*w*, 1433*m*, 1400*s*, 1204*m*, 1176*w*, 1003*w*, 930*s*, 727*s*. MS (EI, 70 eV): m/z 291/290/289 (M^+ -Br, 10), 210/209/208 (M^+ -2Br, 45), 132/131(M^+ -3Br, 100), 104(30), 78(45). Anal. Calcd. for $C_8H_7Br_3N_2$: C, 25.91, H, 1.90, N, 7.55%. Found: C, 26.13 , H, 1.84 , N, 7.78 .

The second fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (505 mg, 86%) data as before.

The third fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**) (38 mg, 9%) data as before.

4.23 Bromination of Tetrahydroquinoxaline 19 with Bromine (2 eq):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (650 mg, 4.1 mmol) and chloroform (10 mL).

The resulting reaction mixture was kept at reflux temperature for 2 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (410 mg, 70%).

The second fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**) (20 mg, 5%).

4.24 Bromination of Tetrahydroquinoxaline 19 with Bromine (3 eq):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (1.00 g, 6.3 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 2.5 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,5,8,8-tetrabromo-5,6,7,8-tetrahydroquinoxaline (**23**) (45 mg, 5%), white solid, mp 156-157 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 2H), 3.27 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 146.1, 59.6, 45.7. IR (KBr, cm^{-1}): 3054*w*, 2972*w*, 2914*w*, 2846*w*, 1436*m*, 1393*m*, 1343*w*, 1202*m*,1107*w*, 1033*w*, 931*s*, 749*s*. MS (EI, 70 eV): m/z 289/287/285 (M^+ -2Br, 55), 233 (20), 153 (15), 100 (20), 75 (100). Anal. Calcd. for $C_8H_6Br_4N_2$: C, 21.36, H, 1.34, N, 6.23%. Found: C, 21.66 , H, 1.50, N, 5.97.

The second fraction was 5,5,8-tribromo-5,6,7,8-tetrahydroquinoxaline (**22**) (635 mg, 85%).

The third fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (45 mg, 8%).

The fourth fraction was 5-bromoquinoxaline (**9**) (10 mg, 2%).

4.25 Bromination of Tetrahydroquinoxaline 19 with Bromine (3 eq):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (1.00 g, 6.3 mmol) and chloroform (10 mL). The

resulting reaction mixture was kept at reflux temperature for 2.5 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,5,8,8-tetrabromo-5,6,7,8-tetrahydroquinoxaline (**23**) (45 mg, 5%) data as before.

The second fraction was 5,5,8-tribromo-5,6,7,8-tetrahydroquinoxaline (**22**) (450 mg, 60%) data as before.

The third fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (90 mg, 15%) data as before.

4.26 Bromination of Tetrahydroquinoxaline 19 with Bromine (6 eq):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **19** (135 mg, 1.0 mmol), bromine (1.00 g, 6.3 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 3 h. The residue was purified via column chromatography on silica gel (20 g) by eluting with 15% EtOAc/*n*-hexane. 5,5,8,8-Tetrabromo-5,6,7,8-tetrahydroquinoxaline (**23**) (450 mg, 99%) was obtained as a sole product.

4.27 Bromination of Tetrahydroquinoxaline 19 with Bromine (6 eq):

The reaction was carried out by the general procedure described in section 4.1.1 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (2.00 g, 12.5 mmol) and chloroform (10 mL). The resulting reaction mixture was kept at reflux temperature for 3 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The second fraction was 5,5,8,8-tetrabromo-5,6,7,8-tetrahydroquinoxaline (**23**) (680 mg, 75%) data as before.

The third fraction was 5,5,8-tribromo-5,6,7,8-tetrahydroquinoxaline (**22**) (75 mg, 10%) data as before.

4.28 Photochemical Bromination of Tetrahydroquinoxaline 19 with Bromine (1.1 eq):

The reaction was carried out by the general procedure described in section 4.1.2 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (350 mg, 2.2 mmol) and carbon tetrachloride (10 mL). The resulting reaction mixture was kept at reflux temperature for 2 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (90 mg, 15%) data as before.

The second fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**) (300 mg, 70%) data as before.

4.29 Photochemical Bromination of Tetrahydroquinoxaline 19 with Bromine (2.1 eq):

The reaction was carried out by the general procedure described in section 4.1.2 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (650 mg, 4.1 mmol) and carbon tetrachloride (10 mL). The resulting reaction mixture was kept at reflux temperature for 30 min. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (500 mg, 85%) data as before.

The second fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**) (50 mg, 12%) data as before.

4.30 Photochemical Bromination of Tetrahydroquinoxaline 19 with Bromine (3.1 eq):

The reaction was carried out by the general procedure described in section 4.1.2 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (1.00 g, 6.3 mmol) and carbon tetrachloride (10 mL). The resulting reaction mixture was kept at reflux temperature for 45 min. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,5,8-tribromo-5,6,7,8-tetrahydroquinoxaline (**22**) (320 mg, 43%) data as before.

The second fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (80 mg, 14%) data as before.

The third fraction was 5-bromoquinoxaline (**9**) (100 mg, 24%) data as before.

4.31 Photochemical Bromination of Tetrahydroquinoxaline 19 with Bromine (4.1 eq):

The reaction was carried out by the general procedure described in section 4.1.2 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), bromine (1.32 g, 8.3 mmol) and carbon tetrachloride (10 mL). The resulting reaction mixture was kept at reflux temperature for 45 min. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,6,7,8-tetrabromo-5,6,7,8-tetrahydroquinoxaline (**23**) (480 mg, 53%) data as before.

The second fraction was 5,8-dibromoquinoxaline (**12**) (185 mg, 32%) data as before.

The third fraction was 5-bromoquinoxaline (**9**) (20 mg, 5%) data as before.

4.32 Bromination of Tetrahydroquinoxaline 19 with NBS (6 eq):

The reaction was carried out by the procedure described in section 4.7 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), NBS (4.48 g, 12.5 mmol) and acetonitrile (10 mL). The resulting reaction mixture was kept at reflux temperature for 2 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (320 mg, 55%) data as before.

The second fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**) (150 mg, 35%) data as before.

4.33 Bromination of Tetrahydroquinoxaline 19 with NBS (6 eq):

The reaction was carried out by the procedure described in section 4.7 using tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), NBS (4.48 g, 12.5 mmol) and chloroform (10 mL). The resulting reaction mixture

was kept at reflux temperature for 2 h. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (235 mg, 40%) data as before.

The second fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**) (85 mg, 20%) data as before.

4.34 Bromination of Tetrahydroquinoxaline 19 with NBS (6 eq):

A solution of tetrahydroquinoxaline **19** (270 mg, 2.0 mmol), NBS (4.48 g, 12.5 mmol) and benzoyl peroxide (catalytic amount) in CCl_4 (10 mL) was irradiated with a 500-W lamp in a 25-mL flask equipped with a reflux condenser. The reaction was monitored by TLC or ^{1}H-NMR spectroscopy. After 2h, the resulting reaction mixture was allowed to cool to room temperature and diluted with a saturated solution of sodium carbonate (10 mL). The mixture was extracted with methylene chloride (2x25 mL) and combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromo-5,6,7,8-tetrahydroquinoxaline (**21**) (245 mg, 42%) data as before.

The second fraction was 5-bromo-5,6,7,8-tetrahydroquinoxaline (**20**) (78 mg, 18%) data as before.

4.35 Reaction of Tetrabromide 23 with DBU:

DBU (170 mg, 165 mmL, 1.1 mmol) was added dropwise to a solution of the tetrabromide **23** (225 mg, 0.5 mmol), in dry THF (20 mL) in dark and the resulting reaction mixture was stirred for overnight at room temperature. The solvent was evaporated, the mixture was diluted with a solution of sodium hydroxide (10%, 10 mL) and the aqueous solution was extracted with methylene chloride (3x25 mL). Combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (20 g) by eluting with 15% EtOAc/*n*-hexane. 5,8-Dibromoquinoxaline **(12)** (142 mg, 99%) was obtained as a sole product.

4.36 Reaction of Tribromide 22 with DBU:

The reaction was carried out by the procedure described in section 4.35 using tribromide **22** (185 mg, 0.5 mmol), DBU (170 mg, 165 mmL, 1.1 mmol) and THF (20 mL). The residue was purified via column chromatography on silica gel (20 g) by eluting with 15% EtOAc/*n*-hexane. 5-bromoquinoxaline **(9**) (103 mg, 99%) was obtained as a sole product.

4.37 Reaction of Monobromide 20 with DBU:

The reaction was carried out by the procedure described in section 4.35 using monobromide **20** (210 mg, 1.0 mmol), DBU (450 mg, 440 mmL, 3.0 mmol) and THF (20 mL). The resulting reaction mixture was kept at reflux temperature for overnight. The residue was purified via column chromatography on neutral aluminium oxide (20 g) by eluting with CH_2Cl_2/MeOH (98:2). 5,6-Dihydroquinoxaline **(24**) (120 mg, 92%) was obtained as a sole product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, A part of AB system, J = 2.7 Hz, 1H), 8.20 (d, B part of AB system, J = 2.7 Hz, 1H), 6.61 (dt, A part of AB system, J = 9.8 Hz and 1.7 Hz, 1H), 6.43 (dt, B part of AB system, J = 9.8 Hz and 4.3 Hz, 1H), 3.08 (t, J = 8.4 Hz, 2H), 2.55 (tdd, J = 8.4 Hz, 4.3 Hz and 1.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 148.9, 141.9, 141.2, 135.6, 128.0, 29.5, 23.0. IR (KBr, cm^{-1}): 3045*m*, 2937*m*, 2889*w*, 2829*w*, 1426*s*, 1414*s*, 1378*m*, 1176*m*, 1155*m*, 1133*m*, 852*m*, 713*m*. MS (EI, 70 eV): m/z 133/132/131 (M^+, 100), 105 (20), 78 (20), 67(10). Anal. Calcd. for $C_8H_8N_2$: C, 72.70, H, 6.10, N, 21.20%. Found: C, 72.81 , H, 6.26 , N, 21.31.

4.38 Bromination of 5,6-Dihydroquinoxaline (24) at rt:

Bromine (960 mg, 0.31 mL, 6.0 mmol) was added dropwise to a magnetically stirred solution of 5,6-dihydroquinoxaline (**24**) (132 mg, 1.0 mmol) in chloroform (15 mL) and the resulting reaction mixture was stirred for 15h at room temperature. The mixture was diluted with saturated solution of sodium carbonate (10 mL) and the mixture was extracted with methylene chloride (2x25 mL). Combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (20 g) by eluting with 20% EtOAc/*n*-hexane. 5,6-Dibromo-5,6,7,8-tetrahydroquinoxaline (**25**) (280 mg, 96%) was obtained as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48-8.41 (m, 2H), 5.63-5.57 (m, 1H), 4.97-4.89 (m, 1H), 3.49-3.33 (m, 1H), 3.22-3.09 (m, 1H), 2.99-2.85 (m, 1H), 2.38-2.24 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 148.2, 144.4, 142.9, 50.5, 49.8, 27.1, 24.8. IR (KBr, cm^{-1}) 3047*w*, 2952*w*, 2917*w*, 2852*w*, 1426*m*, 1405*s*, 1133*m*, 1056*m*, 918*m*, 736*m*. MS (EI, 70 eV): m/z 294/292/290 (M^+, 3), 212/210 (M^+ -Br, 10), 132/131 (M^+ -2Br, 100), 104 (20), 77 (25). Anal. Calcd. for $C_8H_8Br_2N_2$: C, 32.91, H, 2.76, N, 9.59%. Found: C, 33.05, H, 2.81, N, 9.42.

4.39 Bromination of 5,6-Dihydroquinoxaline (24) at 82°C:

Bromine (960 mg, 0.31 mL, 6.0 mmol) was added dropwise to a magnetically stirred refluxing solution of 5,6-dihydroquinoxaline (**24**) (132 mg, 1.0 mmol) in acetonitrile (20 mL) at room temperature. The resulting reaction mixture was heated at reflux temperature for 3h. The resulting reaction mixture was allowed to warm to room temperature and the solvent was evaporated. The mixture was diluted with a saturated solution of sodium carbonate (10 mL) and the mixture was extracted with methylene chloride (2x25 mL). Combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane.

The first fraction was 5,8-dibromoquinoxaline (**12**) (64 mg, 22%) data as before.

The second fraction was 5-bromoquinoxaline (**9**) (95 mg, 44%) data as before.

The third fraction was quinoxaline (**1**) (20 mg, 15%) data as before.

4.40 Synthesis of Quinoxaline-1,4-dioxide (26)

To a magnetically stirred solution of quinoxaline (**1**) (2.60 g, 20.0 mmol) in chloroform (150 mL) was added *m*-CPBA (13.45 g, 77%, 60.0 mmol) portionwise at 0 °C. The reaction mixture was stirred for 48*h* at room temperature. The mixture was diluted with a solution of sodium hydroxide (10%, 20 mL) and extracted with methylene chloride (3x50 mL). The combined organic layers were washed with saturated brine (2 x 30 mL), water, dried over Na_2SO_4, and filtered. The solvent was removed in vacuo.

Quinoxaline-1,4-dioxide (**26**),[20f,28] (3.20 g, 99%) was obtained as a pure product (Yellow solid, mp 241-242 °C, lit.[20f] mp 241-243 °C).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (AA' part of AA'BB' system, 2H), 8.26 (s, 2H), 7.88 (BB' part of AA'BB' system, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 132.2, 130.5, 120.5. IR (KBr, cm^{-1}) 3048*w*, 1642*b*, 1524*m*, 1373*s*, 1287*m*, 1233*m*, 1086*w*, 815*m*, 778*s*.

4.41 Synthesis of Quinoxaline-1-oxide (29):

The reaction was carried out by the procedure described in section 4.40 using quinoxaline (**1**) (2.60 g, 20.0 mmol), *m*-CPBA (4.93 g, 77%, 22.0 mmol) and chloroform (150 mL). The residue was purified via column chromatography on silica gel (100 g) by eluting with MeOH/CH_2Cl_2 (1:24).

The first fraction was quinoxaline-1-oxide (**29**)[29] (2.25 g, 77%), white solid, mp 125 °C (lit.[20f] mp 122-123 °C).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, J = 3.5 Hz, 1H), 8.57 (bd, J = 8.5 Hz, 1H), 8.35 (d, J = 3.5 Hz, 1H), 8.12 (bd, J = 8.5 Hz, 1H), 7.82 (bd, J = 8.5 Hz, 1H), 7.75 (bd, J = 8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 145.9, 137.5, 131.7, 130.2, 130.1, 129.2, 118,9. IR (KBr, cm^{-1}): 3096*m*, 1642*w*, 1576*s*, 1500*s*, 1380*m*, 1363*m*, 1318*s*, 1262*w*, 1130*w*, 890*m*, 759*s*. Anal. Calcd. for $C_8H_6N_2O$: C, 65.75, H, 4.14, N, 19.17%. Found: C, 66.10, H, 4.27, N, 18.80.

The second fraction was quinoxaline-1,4-dioxide (**26**) (300 mg, 9%) data as before.

4.42 Synthesis of 5-Bromoquinoxaline-1-oxide (31)

The reaction was carried out by the procedure described in section 4.40 using 5-bromoquinoxaline (**9**) (210 mg, 1.0 mmol), *m*-CPBA (675 mg, 77%, 3.0 mmol) and chloroform (20 mL). The residue was purified via column chromatography on silica gel (20 g) by eluting with 40% EtOAc/*n*-hexane and 5-bromoquinoxaline-1-oxide **(31**) was obtained as a white solid (224 mg, 99%, mp 174-175 °C).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 3.5 Hz, 1H), 8.53 (d, J = 8.1 Hz, 1H), 8.36 (d, J = 3.5 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.58 (t, J = 8.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 143.6, 138.8, 135.5, 130.2, 129.4, 125.1, 118.8. IR (KBr, cm^{-1}): 3076*w*, 3048*w*, 2924*w*, 1569*m*, 1489*s*, 1378*s*, 1311*s*, 892*s*, 799*s*. MS (EI, 70 eV): m/z 225/224(M^+, 30), 209/208(M^+ -O, 45), 181(15), 155(20), 129 (M^+ -O, -Br, 10), 118(25), 91(30), 75 (100). Anal. Calcd. for $C_8H_5BrN_2O$: C, 42.70, H, 2.24, N, 12.45%. Found: C, 42.47, H, 2.70, N, 11.99.

4.43 Reaction of Quinoxaline-1,4-dioxide (26) with $POBr_3$ (2.9 eq)

A solution of $POBr_3$ (1.67 g, 5.8 mmol) in methylene chloride (200 mL) was added dropwise to a magnetically stirred solution of quinoxaline-*N*-oxide (325 mg gr, 2.0 mmol) **26** in mixture of methylene chloride (10 mL) and triethylamine (510 mg, 5.0 mmol). The resulting mixture was stirred for 30 min. at room temperature and 1*h* at 40°C. The mixture was diluted with solution of sodium hydroxide (10%, 10 mL) and the aqueous solution was extracted with methylene chloride (2x50 mL). Combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (50 g) by eluting with 10% EtOAc/*n*-hexane.

The first fraction was 2,3-dibromoquinoxaline (**27**), white solid, mp 157-159 °C. 475 mg, 82%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (AA' part of AA'BB' system, 2H), 7.82 (s, 2H), 7.88 (BB' part of AA'BB' system, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 140.8, 131.3, 128.4. IR (KBr, cm^{-1}): 3098*w*, 3035*m*, 2924*w*, 1656*w*, 1514*m*, 1257*m*, 1110*w*, 1078*w*, *960s*, 771*s*. Anal. Calcd. for $C_8H_4Br_2N_2$: C, 33.37, H, 1.40, N, 9.73%. Found: C, 33.75, H, 1.44, N, 9.78.

The second fraction was quinoxaline (**1**), 45 mg, 17% data as before.

4.44 Reaction of Quinoxaline-1,4-dioxide (26) with $POBr_3$ (1 eq) at 40 °C:

The reaction was carried out by the procedure described in section 4.43 using quinoxaline-1,4-dioxide (**26**) (325 mg, 2.0 mmol), NEt_3 (245 mg, 2.4 mmol), $POBr_3$ (575 mg, 5.8 mmol) and methylene chloride (30 mL). The resulting mixture was stirred for 30 min. at room temperature and 1 h at 40°C. The residue was purified via column chromatography on silica gel (50 g) by eluting with 10% EtOAc/*n*-hexane.

The first fraction was 2,3-dibromoquinoxaline (**27**), 115 mg, 20% data as before.

The second fraction was 2-bromoquinoxaline (**28**), white solid, mp 58-60 °C (lit.[31c] mp 58 °C), 105 mg, 25%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.11-8.06 (m, 1H), 8.05-7.99 (m, 1H), 7.81-7.76 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 143.2, 141.1, 139.4, 131.2, 130.3, 129.4, 128.6. IR (KBr, cm^{-1}): 3059*w*, 2925*w*, 1538*m*, 1483*w*, 1125*m*, 1078*s*, 951*m*, 760*s*. MS (EI, 70 eV): m/z 210/208(M^+, 30), 129 (M^+ -Br, 100), 102 (70), 76(35). Anal. Calcd. for $C_8H_5BrN_2$: C, 45.97, H, 2.41, N, 13.40%. Found: C, 46.37, H, 2.68, N, 12.96.

The third fraction was quinoxaline-1-oxide (**29**), 132 mg, 45% data as before.

4.45 Reaction of Quinoxaline-1,4-dioxide (26) with $POBr_3$ (1 eq) at rt:

The reaction was carried out by the procedure described in section 4.43 using quinoxaline-1,4-dioxide (**26**) (325 mg, 2.0 mmol), NEt_3 (245 mg, 2.4 mmol), $POBr_3$ (575 mg, 5.8 mmol) and methylene chloride (30 mL). The resulting mixture was stirred for 2 h at room temperature. The residue was purified via column chromatography on silica gel (50 g) by eluting with 10% EtOAc/*n*-hexane.

The first fraction was 2,3-dibromoquinoxaline (**27**), 140 mg, 24% data as before.

The second fraction was 3-bromoquinoxaline-1-oxide (**30**), brown oil, 210 mg, 47%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 8.5 Hz, 1H), 8.47 (s, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.88-7.82 (m, 1H), 7.79-7.72 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 138.2, 132.8, 131.5, 130.2, 129.3, 122.9, 119.1. IR (KBr, cm^{-1}): 3065*m*, 2919*w*, 1660*w*, 1574*m*, 1519*w*, 1491*s*, 1448*w*, 1420*m*, 1334*s*, 1247*m*, 1093*w*, 915*m*. MS (EI, 70 eV): m/z 225/223 (M^+, 30), 210/208 (M^+ -O, 20), 130(100), 102 (40), 90(35), 75(45). Anal. Calcd. for $C_8H_5BrN_2O$: C, 42.70, H, 2.24, N, 12.45%. Found: C, 43.08, H, 2.71 , N, 11.99.

The third fraction was quinoxaline (**1**), 52 mg, 20% data as before.

4.46 Reaction of Quinoxaline-1-oxide (29) with $POBr_3$ (1.45 eq) at rt:

The reaction was carried out by the procedure described in section 4.43 using quinoxaline-1,-oxide (**29**) (290 mg, 2.0 mmol), NEt_3 (260 mg, 2.6 mmol), $POBr_3$ (825 mg, 2.9 mmol) and methylene chloride (30 mL). The resulting mixture was stirred for overnight at room temperature. The residue was purified via column chromatography on silica gel (20 g) by eluting with 10% EtOAc/*n*-hexane. 2-Bromoquinoxaline **(28**) (410 mg, 99%) was obtained as a sole product.

4.47 Reaction of 5-Bromoquinoxaline-1-oxide (31) with $POBr_3$

The reaction was carried out by the procedure described in section 4.43 using 5-bromoquinoxaline-1-oxide (**31**) (225 mg, 1.0 mmol), NEt_3 (150 mg, 1.5 mmol), $POBr_3$ (575 mg, 2.0 mmol) and methylene chloride (20 mL). The resulting mixture was stirred for overnight at room temperature. The residue was recrystallized from mixture of CH_2Cl_2/*n*-hexane (1:4) and 2,5-dibromoquinoxaline (**32**) was obtained as a red solid (285 mg, 99%, mp 157-158 °C).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.09 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.65 (dd, J = 8.5 Hz and J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 144.0, 140.4, 139.0, 133.9, 131.5, 128.4, 124.2. IR (KBr, cm^{-1}): 3032*w*, 1594*w*, 1537*m*, 1451*w*, 1382*w*, 1320*w*, 1253*w*, 1153*w*, 1092*m*, 1050*w*, 962*s*. MS (EI, 70 eV): m/z 288/286//284 (M^+, 35), 209/207(M^+ -Br, 70), 181 (30), 128(55), 100 (60), 76(70). Anal. Calcd. for $C_8H_4Br_2N_2$: C, 33.37, H, 1.40, N, 9.73%. Found: C, 33.79, H, 1.55, N, 9.73.

4.48 Reaction of 5,6-dibrom-5,6,7,8-tetrahydroquinoxaline (25) with DDQ:

DDQ (690 mg, 2.5 mmol) was added to a magnetically stirred solution of 5,6-dibromo-5,6,7,8-tetrahydroquinoxaline **(25)** (250 mg, 0.85 mmol) in benzene (15 mL). The resulting reaction mixture was heated at reflux temperature for 7h. After the reaction was completed, the resulting reaction mixture was allowed to warm to room temperature and filtered. The mixture was diluted with saturated solution of potassium bicarbonate (10 mL) and the mixture was extracted with ethyl acetate (2x25 mL).

Combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified via column chromatography on silica gel (50 g) by eluting with 15% EtOAc/*n*-hexane and 5-bromoquinoxaline (**9**) was obtained as a white solid (22 mg, 12%).

4.49 Reaction of A mixture of 6-Bromo-1,2,3,4-tetrahydroquinoxaline (16) and 6,7-Dibromo-1,2,3,4-tetrahydroquinoxaline (17) with DDQ:

The reaction was carried out by the procedure described in section 4.48 using a mixture of 6-bromo-1,2,3,4-tetrahydroquinoxaline (**16**) (850 mg, 4.0 mmol) and 6,7-dibromo-1,2,3,4-tetrahydroquinoxaline **(17)** (150 mg, 0.5 mmol), DDQ (3.06 g, 13.5 mmol) and benzene (30 mL). The resulting mixture was refluxed for 5h.

6,7-dibromoquinoxaline (**13**) was separated by crystallization from methanol (103 mg) data as before.

6-Bromoquinoxaline (**10**) was obtained by sublimating of the remaining part of residue at 125 °C (500 mg) data as before.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2016……..

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