QUINOXALINE SYNTHESIS BY DOMINO REACTIONS

DOI: http://dx.medra.org/10.17374/targets.2018.21.98

Jie-Ping Wan and Li Wei

College of Chemistry and Chemical Engineering, Jiangxi Normal University, 330022 Nanchang, P.R. China (e-mail: wanjieping@jxnu.edu.cn)

Abstract. *Quinoxalines are highly useful heterocyclic compound showing important application in organic synthesis and many other areas. Researches on the synthesis of quinoxalines have received tremendous advances in the past decade. Herein, the advances in the quinoxaline synthesis, including the traditional vicinal diketone condensation, synthesis using precursors such as o-nitroanilines, as well as miscellaneous approaches with other novel building blocks.*

Contents

1. Introduction

Quinoxalines are a class of conventional heterocyclic aryl compounds containing two cycles and two nitrogen atom in one of the two rings. The quinoxaline skeleton is attractive since it occurs frequently in pharmaceutically and biologically relevant organic compounds (Figure 1). For example, XK469 is an active agent with promising antitumor activity,[1] UK 14304 is α-adrenoceptor agonist,[2] the simple methoxyl and phenyl functionalized quinoxaline S AG-1296 is commercial inhibitor of U-protein tyrosine kinase, to name but a few.[3]

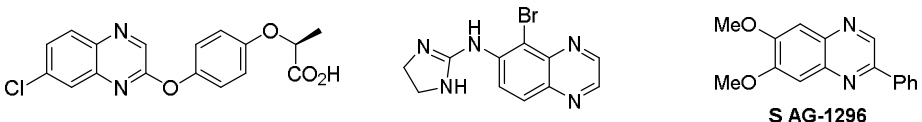


Figure 1. Biological relevant quinoxalines.

Owing to the significant potential of the privileged heterocyclic backbone in discovering new lead compounds and drugs, the synthesis quinoxaline has attracted longstanding interest. Traditionally, the synthesis of quinoxalines could be accessed via the condensation of *o*-phenylenediamines and precursors with vicinal diketones, α-hydroxyl ketones and α-halogen ketones etc. Notably, following the rapid advances in modern synthetic and catalytic technologies, there are also a number of novel synthetic methods that have been devised for the synthesis of quinoxalines in more diverse and facile manner. Herein, we provide a comprehensive overview in the research advances of quinoxaline synthesis over the past decade. According

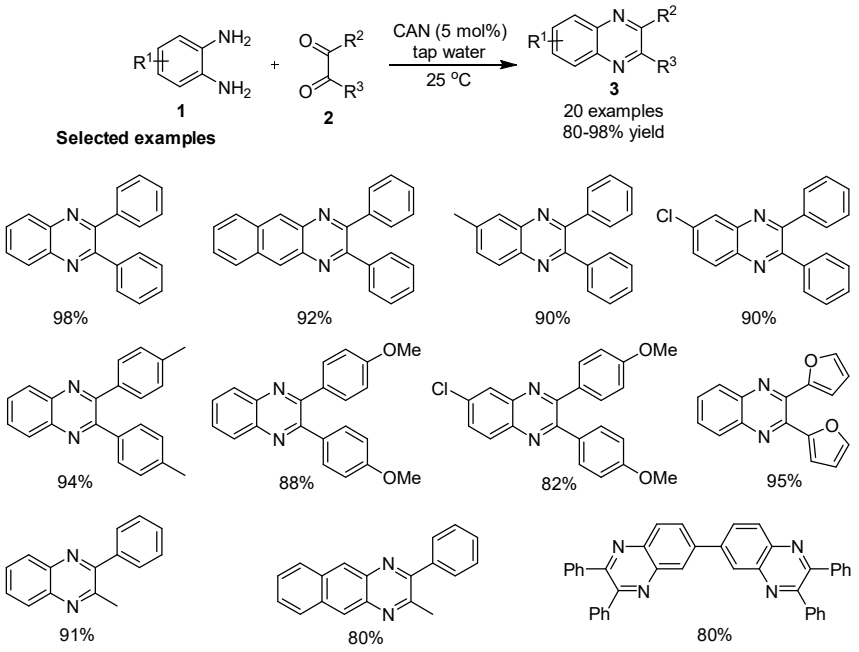
to the known literature, both the syntheses with conventional vicinal diamine condensation as well as those novel synthetic methods employing simpler starting materials are covered.

2. Synthesis using *o*-phenylenediamine as the main building block

o-Phenylenediamine is the most frequently employing building block in the synthesis of quinoxalines, it is able to incorporated different carbonyl substrates such as vicinal diketones, α-hydroxyl ketones, α-haloketone and even unfunctionalized methylene ketones to provide quinoxalines. The following contents summarize the representative advances of the synthetic methods.

2.1. Reaction with vicinal dicarbonyl compounds

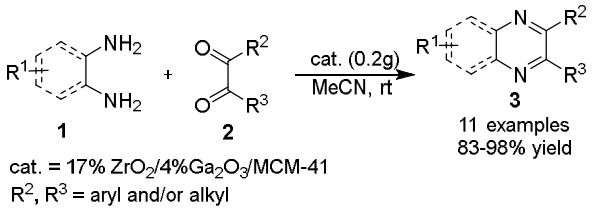
The reaction of *o*-phenylenediamines with vicinal diketones is the earliest known approach toward the synthesis of quinoxalines.[6] The research efforts in this transformation have led to the establishment of many efficient catalytic methods to provide quinoxalines. While various Lewis/Brøsted acids and Lewis bases have been found as effective catalyst for such reactions, the research interest in developing simpler and more sustainable catalytic methods for the this condensation-based quinoxaline synthesis remain as attractive work. Yao and co-workers[7] reported in 2006 the cerium (IV) ammonium nitrate (CAN)-catalyzed synthesis of quinoxalines via the reactions of *o*-phenylenediamines **1** and vicinal diketones **2** by using tap water as medium. As shown in Scheme 1, the reactions were carried out in tap water at room temperature, quinoxalines **3** were provided with generally excellent yield in the presence of 5 mol% CAN. More notably, the products could be easily acquired after reaction by simple filtration and washing with water. The water medium, chromatography-free purification and low catalyst loading featured in this catalyst method made up a high green route to access quinoxalines (Scheme 1).



Scheme 1. Tap water mediated synthesis of quinoxalines using *o*-phenylenediamines and diketones.

Unlike the above efforts in developing green reaction medium, Pandurangan et al[8] prepared the heterogeneous mesoporous ZrO2/MxOy (M = Al, Ga, In and La) mixed metal oxides supported on MCM-41, and this catalyst was found highly practical to catalyze the reactions of *o*-phenylenediamines and vicinal diketones for the synthesis of quinoxalines **3**. The main advantage of this catalyst was the recyclability of the

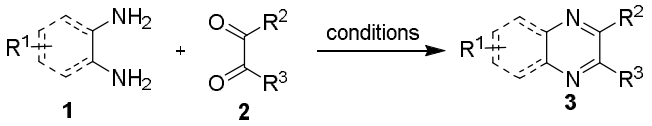
heterogeneous catalyst, which was found with no evident loss in catalytic activity after using 4 times. In addition, the scope of the substrates was also satisfactory. For example, the full alkyl functionalized vicinal diketone such as biacetyl could be smoothly participate the quinoxaline synthesis, and 1,2-ethanediamine was also found applicable for the condensation reaction to provide 2,3-dihydropyrazine products (Scheme 2).



Scheme 2. Quinoxaline synthesis catalyzed by MCM-41 supported heterogeneous catalyst.

Additionally, the efforts in developing reusable catalyst also led to the discovery of the many other heterogeneous catalysts which could be practically applied to this kind of quinoxaline synthesis. Liu and co-workers[9] employed amberlyst-15 as the heterogeneous catalyst, and realized the reactions of **1** and **2** to provide **3** by heating at 70 ^{o}C in water. The insoluble amberlyst could be easily recovered by filtration, ether washing and air drying, and recovered catalyst was used repeatedly 5 times without losing catalytic activity (Scheme 3). On the other hand, Salunkhe et al[10] developed the catalytic system consists of Brøsted acid hydrotrope combined catalyst (BAHC) and aqueous medium for similar reactions. The recoverable catalyst made up of PTSA and sodium *p*-toluene sulfonate (NaPTS) exhibited satisfactory catalytic application of the synthesis of quinoxalines using mainly *o*-phenylenediamines and di-aryl functionalized vicinal diketones, and alkyl substrates in the reaction were not defined. The catalyst in aqueous phase could be recovered by moving the water after filtration, and only slight loss in the catalytic activity was observed after 5 runs (Scheme 3). Tilve and co-workers[11] observed that Graphite was also an efficient promoter for the construction of quinoxaline **3** via the condensation of **1** and **2**. In the presence of Graphite and, the quinoxaline products could synthesized with broad diversity via the employing of various diamines and vicinal diketiones. Notably, using α-hydroxyl ketone as the alternative substrate of vicinal diketone was also able to afford the target quinoxaline product in the protocol. Although the Graphite was used in 2 equiv. mole amount, it could also be easily recovered via filtration and drying (heating at 100 ^{o}C), and no evident decrease in the yield of product was found by running the reactions for 6 times using the recycled catalyst (Scheme 3). Brahmachari et al[12] employed the magnetically recyclable $MnFe_2O_4$ nano-material as catalyst to enable the facile synthesis of benzimidazoles and quinoxaline via the condensation of vicinal diamines and aldehydes, 1,2-diketiones, respectively. The synthesis of quinoxaline products could be performed with good results at room temperature in the presence of this magnetic catalyst (Scheme 3). More recently, Baghbanian[13] disclosed that the nanozeolite clinoptilolite functionalized with propylsulfonic acid (NZ-PSA) was also a practical heterogeneous catalyst for the synthesis of qunoxalines via this condensation reaction. The synthesis of various quinoxalines from the reactions of different o-phenylenediamines and cyclic/acyclic 1,2-diketones. These reactions were also run in water at room temperature to provide quinoxaline products with excellent yields, and the catalyst could be recycled and reused for eight times without evident loss in catalytic activity. Notaly, the alternative synthesis of quinoxaline products via the reactions of α-bromoketones and *o*-phenylenedimines could also be realized smoothly in the presence of this catalyst (Scheme 3).

As for the similar reactions employing conventional acidic or basic catalyst, or even catalyst-free synthesis, there are also plenty of reports occurred in recent several years. As some examples of recent work, Table 2 summarized some typical results on quinoxaline synthesis under different reaction conditions. Wang et al[14] reported the synthesis of quinoxalines via the irradiation CEM-focused microwave in the presence of 15% mole PEG-400, and quinoxaline products were synthesized with broad substrate scope and generally excellent yield (Table 1). Narsaiah and Kumar[15] developed the synthetic method employing cerium chloride and glycerine as reaction system to enable the synthesis of quinoxalines via identical condensation (Table 1).



Ref. 9, Liu et al: Amberlyst-15 (24 mol%) H_2O, 70 °C — 18 examples, 70->99% yield

Ref. 10, Salunkhe et al: BAHC (5 mol% PTSA and 40 % aq NaPTS, rt — 12 examples, 81->96% yield

Ref. 11, Tilve et al: Graphite (2 equiv.) EtOH, rt — 17 examples, 12-93% yield

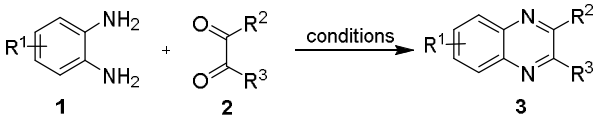
Ref. 12, Brahmachari et al: $MnFe_2O_4$ NP (10 mol%) EtOH, rt — 5 examples, 70-91% yield

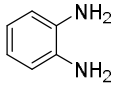
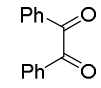
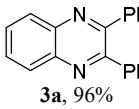
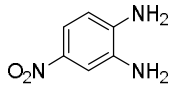
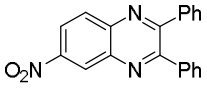
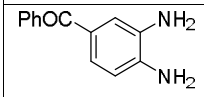
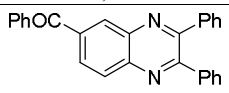
Ref. 13, Baghbanian: NZ-PSA (0.01g/1mmol reaction) water, rt — 10 examples, 88-98% yield

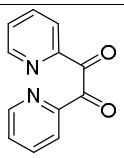
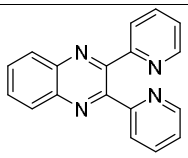
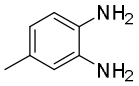
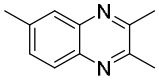
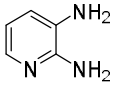
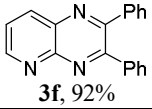
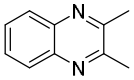
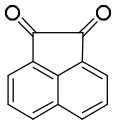
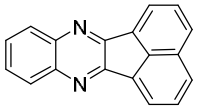
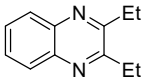
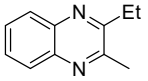
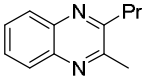
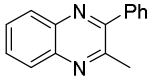
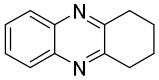
Scheme 3. Synthesis of quinoxaline with recyclable heterogeneous catalyst.

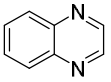
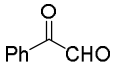
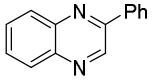
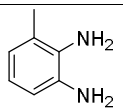
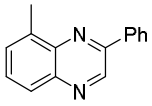
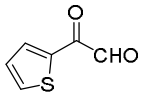
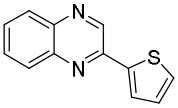
The products were also afforded with satisfactory yields and exhibited tolerance to both aryl and alkyl functionalized vicinal diketones (Table 1). Some more facile methods allowing this condensation-based quinoxaline synthesis were also developed. Micheletti and co-workers[16] synthesized a series of quinoxaline by simply stirring the mixture of o-phenylenediamines and vicinal diketones in water at room temperature. The method was found to specifically applicable for the synthesis using alkyl functionalized 1,2-diketiones (R^2 and/or R^3 = alkyl), and diaryl functionalized diketones (R^2, R^3 = aryl) was no practical substrate for similar quinoxaline synthesis. A notable point of this method was that the synthesis of unsubstituted quinoxaline had been found feasible by employing oxalaldehyde as the dicarbonyl substrate (Table 1). Synthesis of quinoxalines based on this transformation in water was also furnished by employing the surfactant Tween 40 which acted also as microreactor in the reactions.[17] More recently, Lassagne et al[18] investigated the reaction of o-phenylenediamines and diketone/α-ketoaldehydes via the catalysis of ammonium bifluoride (ABF) in mixed MeOH and water, by which a class of 2,3-disubstituted and 2-subsituted quinoxaline were provided up to quantitative yield (Table 1).

Table 1. Selected recent examples on catalytic or catalyst-free quinoxaline synthesis (only selected representative products are given).

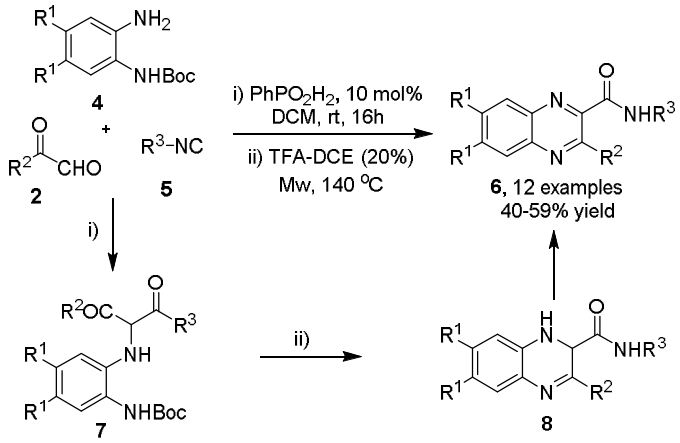


Diamine	Diketone	Conditions	Product (yield)	Reference
 **1a**	 **2a**	PEG-400 (15% mol), Mw, 120 °C	 **3a**, 96%	14
 **1b**	**2a**	PEG-400 (15% mol), Mw, 120 °C	 **3b**, 94%	14
 **1c**	**2a**	PEG-400 (15% mol), Mw, 120 °C	 **3c**, 92%	14

1a	 **2b**	PEG-400 (15% mol), Mw, 120 °C	 **3d**, 94%	14
 **1d**	 **2c**	PEG-400 (15% mol), Mw, 120 °C	 **3e**, 95%	14
1a	**2a**	$CeCl_3 \cdot 7H_2O$ (10 mol%), glycerin, 70 °C	**3a**, 95%	15
 **1e**	**2a**	$CeCl_3 \cdot 7H_2O$ (10 mol%), glycerin, 70 °C	 **3f**, 92%	15
1a	**2c**	$CeCl_3 \cdot 7H_2O$ (10 mol%), glycerin, 70 °C	 **3g**, 90%	15
1b	**2a**	$CeCl_3 \cdot 7H_2O$ (10 mol%), glycerin, 70 °C	**3b**, 84%	15
1a	 **2d**	$CeCl_3 \cdot 7H_2O$ (10 mol%), glycerin, 70 °C	 **3h**, 92%	15
1a	**2c**	water, rt	**3g**, 95%	16
1a	 **2e**	water, rt	 **3i**, 88%	16
1a	 **2f**	water, rt	 **3j**, 95%	16
1a	 **2g**	water, rt	 **3k**, 82%	16
1a	 **2h**	water, rt	 **3l**, 83%	16
1a	 **2i**	water, rt	 **3m**, 70%	16

1a	OHC-CHO **2j**	water, rt	 **3n**, 76%	16
1a	**2a**	ABF (0.5 mol%), MeOH/H_2O (v/v = 4:1), r.t.	**3a**, quant. yield	18
1a	**2h**	ABF (0.5 mol%), MeOH/H_2O (v/v = 4:1), r.t.	**3l**, 97%	18
1a	**2c**	ABF (0.5 mol%), MeOH/H_2O (v/v = 4:1), r.t.	**3g**, 98%	18
1a	 **2k**	ABF (0.5 mol%), MeOH/H_2O (v/v = 4:1), r.t.	 **3o**, quant. yield	18
 **1f**	**2k**	ABF (0.5 mol%), MeOH/H_2O (v/v = 4:1), r.t.	 **3p**, 94%	18
1a	 **2k**	ABF (0.5 mol%), MeOH/H_2O (v/v = 4:1), r.t.	 **3q**, 94%	18

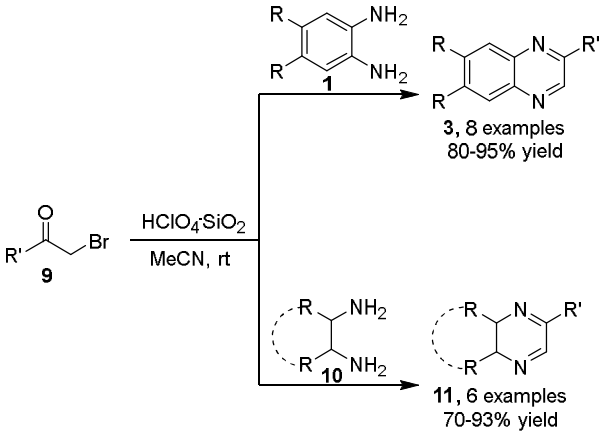
By means of the the condensation of phenylene diamines and vicinal dicarbonyl substrates as well as other tandem transformations, quinoxaline with further elaborated structure could be accessed. Hulme and co-workers[19] devised the one-pot, two step protocol toward the synthesis of quinoxalinyl amides **6** via the assemblies of N-Boc o-phenylenediamine **4**, isocyanides **5** and α-ketoaldehydes **2**. The tandem employment of phenylphosphinic acid ($PhPO_2H_2$) and TFA enable the construction of products **6** via the hemiaminal intermediate **7** and dihydroquinoxaline intermediate **8** (Scheme 4).



Scheme 4. One-pot, two-step synthesis of quinoxalines containing amide substructure.

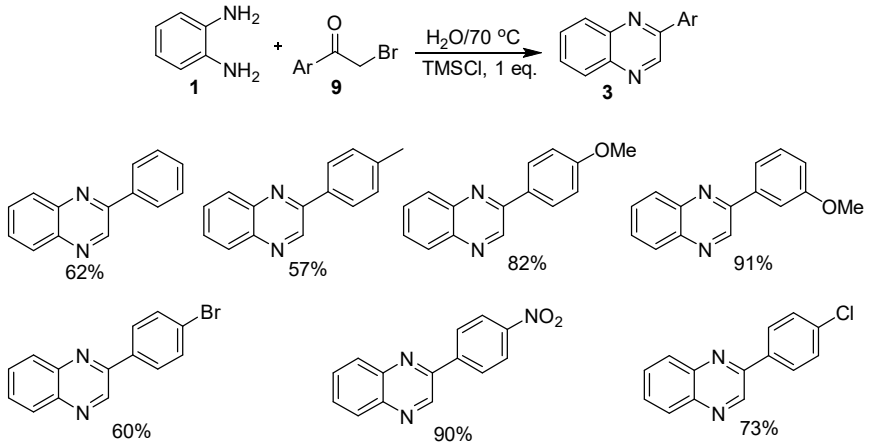
2.2. Reaction with α-haloketones

As typical substrates containing two adjacent electrophilic carbon centers, α-haloketones are tremendously utilized as building blocks in the synthesis of numerous organic products. One such type of the typical products are quinoxalines in which o-phenylenediamines were also the reaction partners. Das et al[20] reported the synthesis of quinoxalines via the reactions of α-bromoketones **9** and phenylenediamines by using $HClO_4 \cdot SiO_2$ as heterogeneous catalyst. As outlined in Scheme 5, both aryl and alkyl α-bromoketones were tolerable to the synthesis to give **3** with excellent yields. On the other hand, using aliphatic vicinal diamines **10** allowed the synthesis corresponding dihydroquinoxalines **10**. The reactions were performed well at room temperature, and the catalyst showed no observable loss in catalytic activity after been recycled and reused for 4 times.



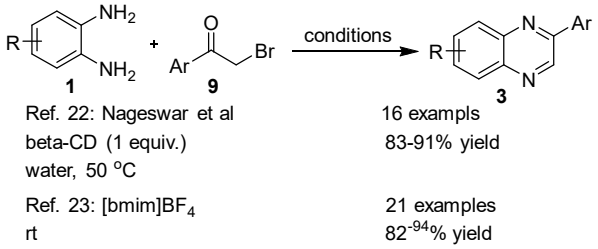
Scheme 5. Synthesis of (dihydro)quinoxalines via the reactions of α-bromoketones and dimines.

Pan and co-worker[21] employed water as medium for the synthesis of quinoxalines in the presence of TMSCl. The reactions proceed well by heating at 70 °C. The mild and simple reaction conditions as well as the only water medium provided a green facile route toward quinoxalines synthesis (Scheme 6).



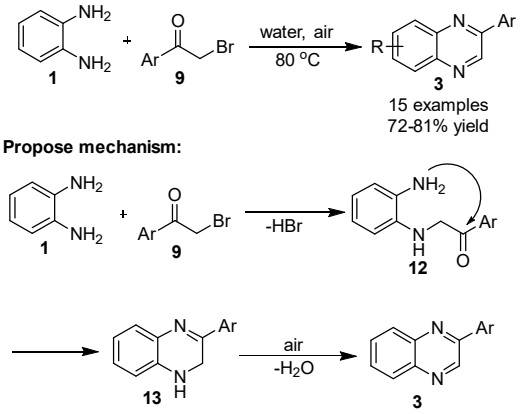
Scheme 6. Quinoxaline synthesis from α-bromoquinoxalines and *o*-phenylenediamines in water.

Subsequently, a variety of different catalytic methods for this transformation were developed. Nageswar and co-workers[22] reported the quinoxaline synthesis via the β-CD (β-cyclodextrin) promoted reactions of **1** ad **9** in which water was used the reaction medium to enable the quinoxaline synthesis by heating at 50 °C (Scheme 7). Meshram et al[23] reported that ionic acid [bmim]BF_4 could mediate the synthesis of quinoxalines **3** via identical reaction without using additional catalyst or additive at room temperature, and the products were all acquired with excellent yield (Scheme 7). Additionally, the Amberlite resin-supported sodium hexafluorophosphate was found to be capable of catalyzing the reactions in aqueous methanol (v/v = 1:1) with satisfactory efficiency and broad tolerance (Scheme 7).[24]



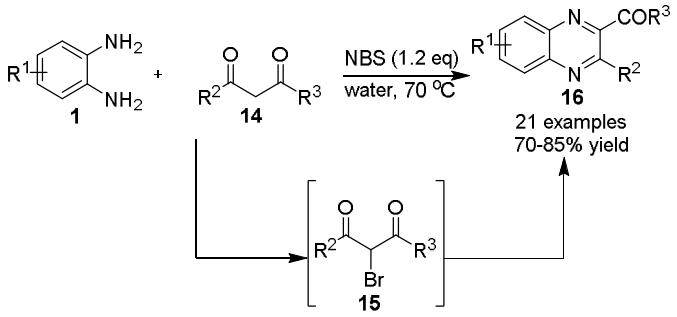
Scheme 7. Different conditions for the synthesis of quinoxaline uisng α-bromoketones.

On the other hand, Nair and co-workers[25] disclosed recently that heating substrates **1** and **9** in water can directly allow the synthesis of quinoxalines **3** under air atmosphere without employing any other reagent. Whilst benefited the simple and green reaction conditions, the scope and yield of the method, however, was inferior than most of those catalytic protocols. The possible mechanism of the reaction consisted of the nucleophilic substitution of the amino group to the alkyl C-Br bond giving intermediate **12**, the intramolecular condensation providing dihydroquinoxaline **13** and the air oxidation to the target product **3** (Scheme 8).



Scheme 8. Water mediate catalyst-free synthesis of quinoxalines.

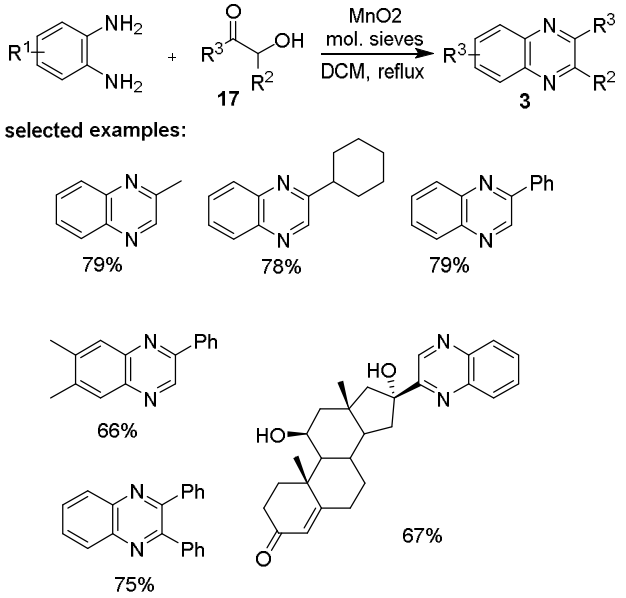
By running the reactions of o-phenylenediamines **1** and 1,3-diketones **14**, Nageswar et al[26] developed a concise route for the synthesis of 2,3-disubstutitued quinoxaline **16** in the presence of NBS in water. The reactions was mediated by the in situ bromination of diketones **14** to generate α-bromodiketones **15** which was analogous with the α-bromoketones **9** in reactivity, thus allowed the construction of products by heating at 70 °C (Scheme 9).



Scheme 9. Water/NBS-mediated synthesis of 2,3-disubstuted quinoxaline by *in situ* bromination.

2.3. Reactions with α-hydroxylated ketones and vicinal diols

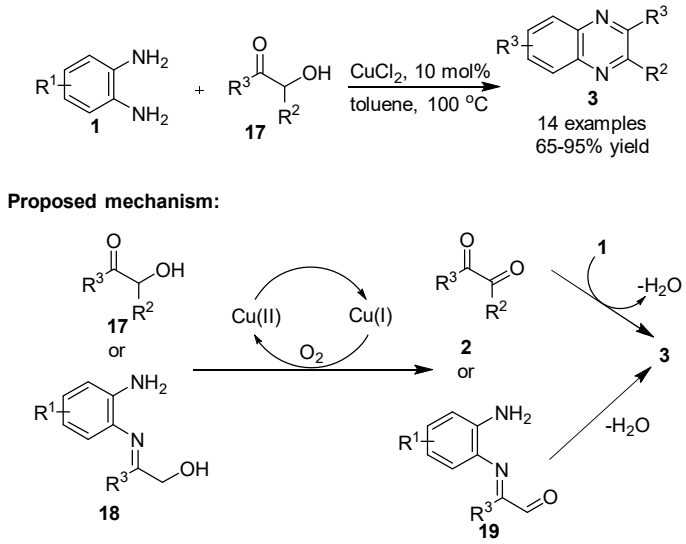
To some extent, the α-hydrxoylated ketones and vicinal diols could both be regarded as the precursors of vicinal diketones. Therefore, they were also employed equivalent building blocks of vicinal diketones in many cases of synthesis such as the quinoxaline synthesis. In 2003, Taylor et al[27] reported the MnO_2-mediated synthesis via the tandem reactions of o-phenylenediamines and α-hydrxoylated ketones **17**. In the presence of mocular sieves and MnO_2, quinoxalines **3** was readily achieved via tandem oxidation and condensation (Scheme 10). This primary result was later on updated by the same group wherein a class of different quinoxaline products using alkyl/aryl functionalized α-hydrxoylated ketones and o-phenylenediamines, by which a more generally applicable catalytic method toward quinoxaline was demonstrated (Scheme 10).[28] The reaction conditions for the same transformation was improved by Chung and co-worker with microwave irradiation using only catalytic loading of MnO_2 under solvent-free conditions, and most of the examined entries could finish in one minute.[29]



Scheme 10. MnO_2-mediated synthesis of quinoxalines.

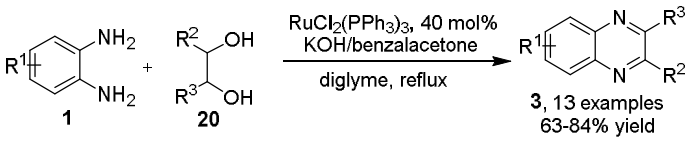
Alternatively, Cho and Oh[30] employed $CuCl_2$ as the catalyst which enabled the reaction with satisfactory yield and scope at 10 mol% loading. The main feature of this catalytic approach was the Cu(II)

might act as the oxidative species enabling the oxidation of the alcohol in **17** or condensed intermediate **18** to carbonyl intermediate **2** or **19** to promote the formation quinoxalines **3**. And the reduced Cu(I) state was regenerated to Cu(II) using oxygen as the terminal oxidant (Scheme 11).



Scheme 11. $CuCl_2$-mediated synthesis of quinoxalines under air.

In addition to these pioneer works, the recent decade witnessed the occurrence of many other catalytic methods for this reaction. Typically examples such as the manganese octahedral molecular sieves,[31] the Ru/C/β-cyclodextrin catalysts,[32] the $FeCl_3$/morpholine,[33] $Ga(ClO_4)_3$/EtOH,[34] the L-prline/water,[35] the heterogeneous gold–carbon nanotube nanohybrid,[36] the Amberlite IR-120H resin,[37] the $Cu(OAc)_2$/TEMPO,[38] propylphosphonic anhydride ($T3P^R$)/DMSO,[39] and PTSA/DMOS[40] etc have all been found as practical catalytic systems in this tandem reaction with individual features in the recyclability of catalyst(s), green reaction medium, mild reaction conditions, high product yield and/or broad substrate scope. By means of similar tandem oxidation and cyclization transformations, vicinal diols were also applicable reaction partners of *o*-phenylenediamines in the synthesis of quinoxalines. Cho and Oh[41] reported the Ru(II)-catalyzed synthesis quinoxaline using o-phenylenediamine and vicinal diols **20** in the presence of KOH and benzalacetone in reflux diglyme. The employment of benzalacetone as hydrogen acceptor was effective in promoting the reaction (Scheme 12). Corma et al investigated the reactions of glycol and analogous vicinal diols with o-phenylenediamines using gold nanoparticles supported on nanoparticulated ceria (Au/CeO_2) or hydrotalcite (Au/HT) as catalysts, which provided quinoxalines **3** with good tolerance by heating at 140 °C in diglyme.[42]



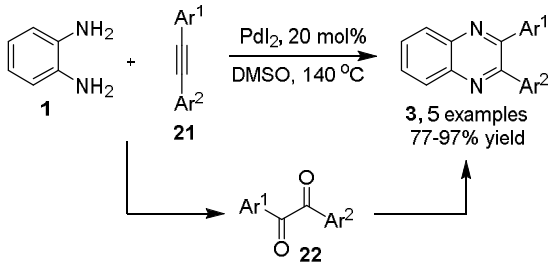
Scheme 12. Ru-catalyzed synthesis of quinoxalines usuing vicinal diols.

2.4. Reactions with alkynes and alkenes

Substrates featuring unsaturated carbon-carbon multiple bonds (double bond and triple bond) are precursors of carbonyl compounds under many different catalytic conditions. Reasonably, substrates such as

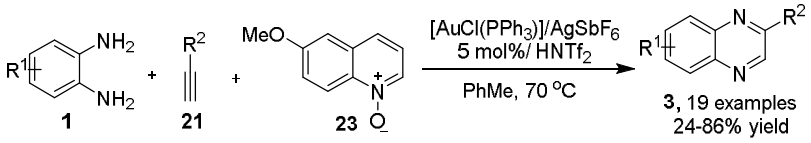
alkynes, alkenes and allenes were also frequently used as building blocks in the construction of quinoxaline heterocycle by incorporating *o*-phenylenediamines.

In 2008, Provot and Alami[43] et al reported the oxidation of alkynes to benzils as well as the one-pot synthesis of quinoxalines via this oxidation by using DMSO-PdI_2 as oxidizing system. This catalytic method allowed the oxidative transformation of alkynes **21** to benzils **22** by heating at 140 °C, and quinoxalines **3** by additionally employing *o*-phenylenediamines (Scheme 13). Later on, Chandrasekhar and co-workers[44] reported an improved catalytic version of this reaction. By applying catalytic amount of $PdCl_2/CuCl_2$ in PEG-400, the oxidative transformation of internal alkynes could be efficiently run to give vicinal diketone **22** at room temperature, and the same condition was practical for the direct synthesis of quinoxalines **3** in the presence of diamine **1**.

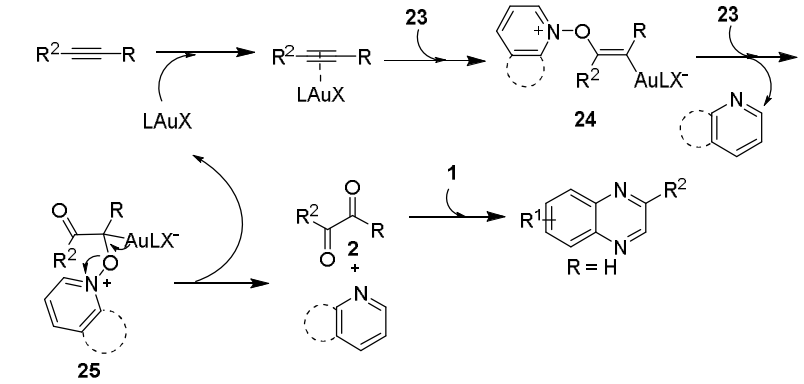


Scheme 13. PdI_2-DMSO promoted quinoxaline synthesis with alkynes and *o*-phenylenediamine.

As different examples employing transition metal catalyst, gold complex was also found as practical catalyst for this kind of quinoxaline synthesis. Hashmi et al[45] reported the synthesis of quinoxalines via $[AuCl(PPh_3)]/AgSbF_6$ co-catalyzed reactions of o-phenylenediamines and terminal alkynes in the presence of quinoline N-oxide **23** which acted as the external oxidant. $HNTf_2$ was employed as additive, and the products generated from both aryl and alkyl alkynes could be synthesized by heating in toluene at 70 °C (Scheme 14).



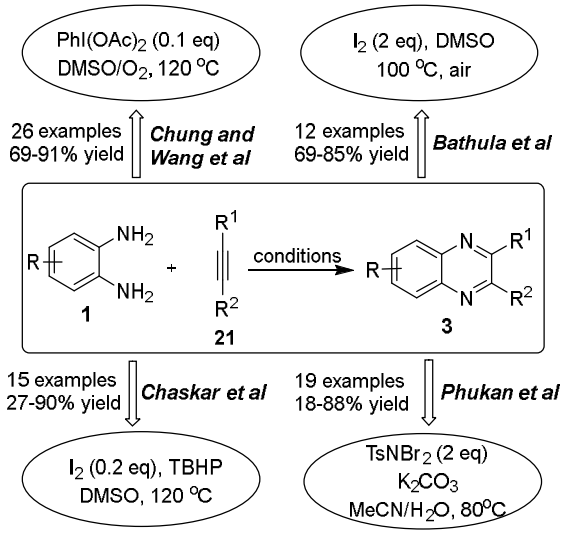
Propsed Mechanism:



Scheme 14. Gold-catalyzed quinoxaline synthesis with alkynes and *o*-phenylenediamine.

As proposed by the authors, the reaction proceeded via the gold assisted oxo-addition of the N-oxide to give intermediate **24**, the additional addition of the N-oxide to **24** and the loss of quinoline providing intermediate **25**, and further release of quinoline as well as the gold species LAuX giving vicinal diketone **2**. The formation of quinoxalines could be achieved via the typical condensation between **1** and **2** (Scheme 14). In addition, $[Ru(cymene)Cl_2]_2$ was also found as an efficient catalyst for the oxidative conversion of terminal alkynes to vicinal diketones and the one-pot synthesis of quinoxalines by subsequent incorporation with o-phenylenediamines.[46]

In parallel with the transition metal-catalyzed systems, developing transition metal-free catalysis of this kind of alkyne oxidation-based quinoxaline synthesis had also received important advances. For example, Chuang and Wang et al[47] developed the $PhI(OAc)_2$-catalyzed synthesis of quinoxalines **3** via the reactions of diamines and terminal alkynes in the presence of oxygen by heating in DMSO at 120 °C (Scheme 15). Bathula and co-workers[48] found that molecular iodine could also mediate this kind of oxidative cascade reactions for quinoxaline synthesis by heating in DMSO at 100 °C and air atmosphere (Scheme 15). In addition, the combination of TBHP and catalytic amount of iodine was reported to be practical system which enabled the formation of quinoxalines via reactions of alkynes and *o*-phenylenediamines (Chaskar et al, Scheme 15).[49] More recently, Phukan and co-workers[50] disclosed that $TsNBr_2$ could mediate the synthesis of quinoxalines via identical starting materials. However, unlike the traditional formation of vicinal diketone intermediates, this synthetic method proceeded via the in situ generated α,α-dibromo ketones from the ketone substrate and $TsNBr_2$ (Scheme 15).

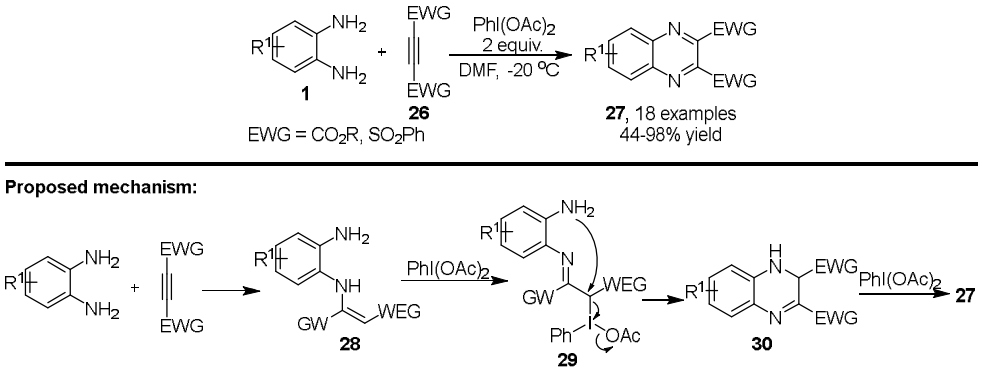


Scheme 15. Transition metal-free quinoxaline synthesis with alkynes and *o*-phenylenediamine.

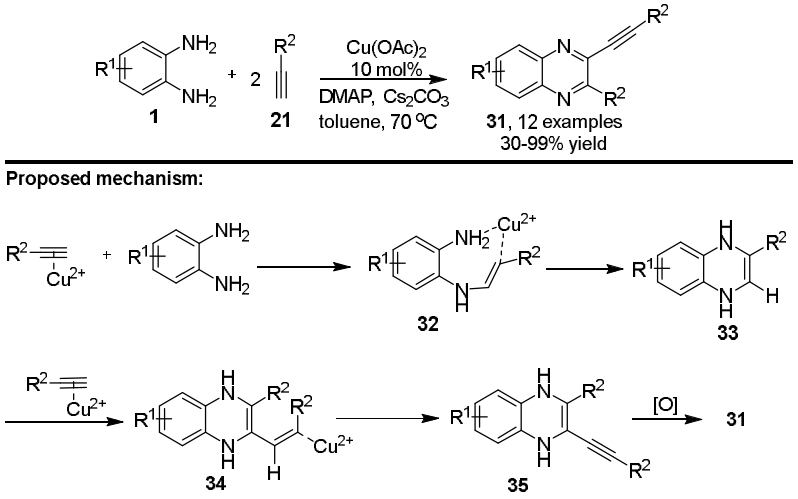
As an extension, the synthesis of quinoxalines **27** was reported by Takeda and Minakata et al[51] via the reactions of o-phenylenediamine and corresponding electron deficient internal alkynes **26**. As displayed in Scheme 16, the reactions were mediated by $PhI(OAc)_2$ in DMF. Based on the authors' assumption, the most possible mechanism was the formation of Michael adduct **28**, the polyvalent iodospecies **29** and the dihydroquinoxaline **30**.

In 2011, Chen and co-workers[52] reported another protocol of quinoxaline synthesis via the reactions of o-phenylenediamine and terminal alkynes. In the reactions, two molecules of alkynes took part in the formation of the alkynyl functionalized quinoxalines **31**. The reactions were performed in the presence of $Cu(OAc)_2$ in toluene by heating at 70 °C. From the viewpoint of the mechanism, the activation of the cupric ion to the C-C triple bond was crucial for the product formation which involved in the addition of the amino group to the alkyne, the copper-mediated oxidative C-H amination of the in situ generated intermediate **32**,

the C-H addition-based alkenylation of **33**, the formation of intermediate **35** via reductive elimination of 34 as well as the oxidative aromatization providing target product (Scheme 17). Later on, Wang et al[53] reported that the Fe_3O_4@Cu_2O–graphene oxide framework with 3D mesoporous structure was a reusable heterogeneous catalyst the this kind of quinoxaline synthesis.



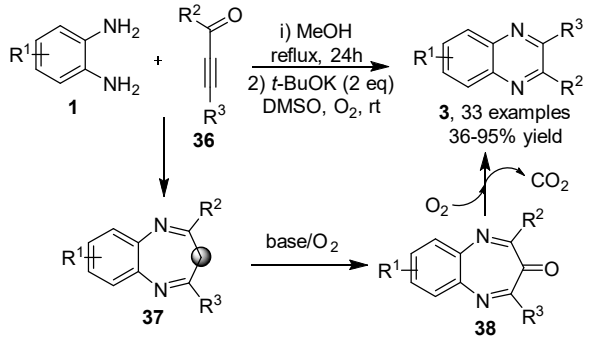
Scheme 16. Quinoxaline synthesis of *o*-phenylenediamines with elelctron deficient internal alkynes.



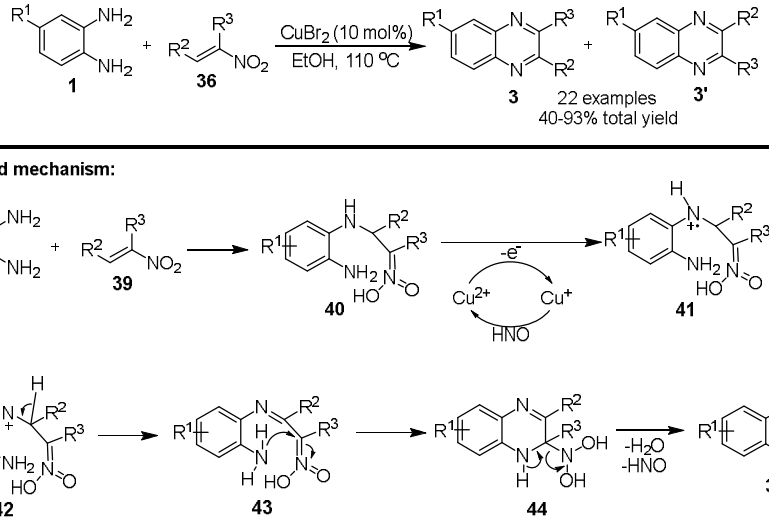
Scheme 17. Synthesis of alkynyl-functionalized quinoxalines.

Cui et al[54] reported another interesting approach toward quinoxaline construction via the reactions of o-phenylenediamine and alkynones **36**. The key process enabling this quinoxaline formation was the oxidative methylene extrusion via intermediates **37** and **38** (Scheme 18).

The C-C double bond in alkenes was also a classical functional group which underwent various oxidation transformations in organic synthesis. Some properly functionalized alkenes such as nitroolefines, enaminones etc, for example, were found as applicable building blocks in the synthesis of quinoxalines. Chen et al[55] employed nitroolefin **39** to react with o-phenylenediamine **1** to provide quinoxalines **3**/**3'** via the catalysis of $CuBr_2$ by heating at 110 °C in EtOH. The reaction started from the aza-Michael addition of the amino group to the nitroolefin which gave intermediate adduct **37**. The oxidation of **40** via Cu^{2+} assisted single electron transfer led to the formation of radical cation **41**. Further oxidation of **41** provided cation species **42**, which underwent subsequent deprotonation, intramolecular nucleophilic addition and extraction of nitro group to yield quinoxaline products via intermediates **43** and **44**, respectively (Scheme 19).



Scheme 18. Quinoxaline synthesis via methylene extrusion.

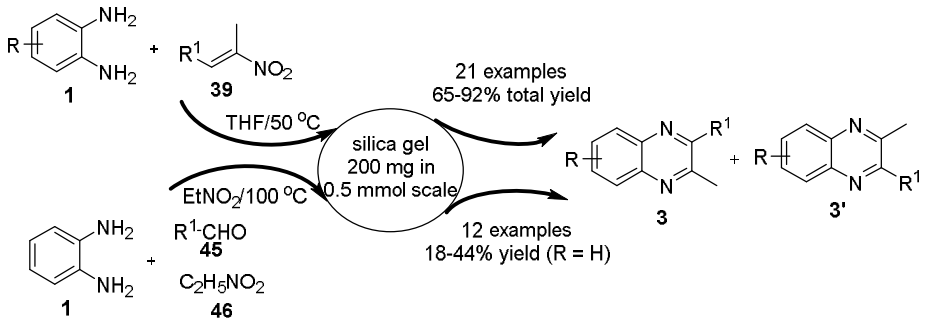


Scheme 19. Synthesis of quinoxalines via the reactions of *o*-phenylenediamines and nitroolefin.

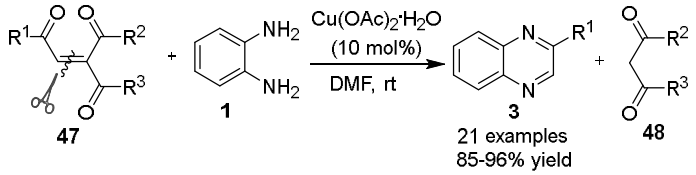
Later on, Zhang and Qi et al[56] developed a complementary catalytic approach for the same kind of synthesis by employing silica gel as catalyst. As outlined in Scheme 19, the reactions of starting materials **1** and **39** proceeded well in THF in the presence of catalytic amount of silica gel by heating at 50 °C. Notably, the direct reactions employing **1**, aldehyde **45** and nitroethane **46** could also provide the quinoxaline products via the in situ formation of nitroolefin with catalysis of silica gel, but the target product were all acquired with very low yield.

Wu and co-workers[57] discovered that he polyfunctionalized alkenes **47** were also effective partners of o-phenylenediamine for the synthesis of quinoxalines. By employing $Cu(OAc)_2$ as catalyst, the formal cleavage of the C-C double bond in substrate **47** enabled the formation of products **3** at room temperature, and the 1,3-dicarbonyl compounds **48** were generated as by-products in the reactions (Scheme 21).

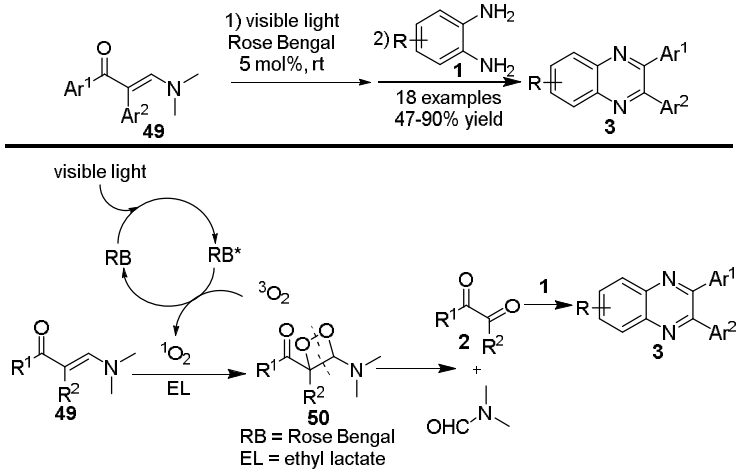
Wan et al[58] employed enaminones **49** as reaction partners to with react with *o*-phenylenediamine, which allowed the synthesis of quinoxalines via visible light irradiation by using 5 mol% Rose Bengal (RB) as the photocatalyst. With this metal-free, photocatalytic protocol, a series of 2,3-diaryl quinoxalines were provided with satisfactory yield. As for mechanism, the reaction was also initiated by the formation of vicinal diketone intermediate. The enaminone **49** was oxidized by oxygen in the presence of RB to give cyclic peroxide intermediate **50** which decomposed to vicinal diketone and enabled the subsequent formation of quinoxaline products **3** (Scheme 22).



Scheme 20. Silica gel catalyzed synthesis of quinoxalines.



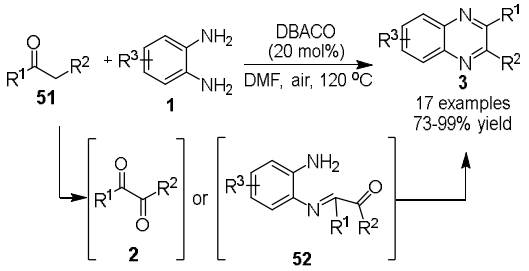
Scheme 21. Quinoxaline synthesis using o-phenylenediamine and tricarbonyl functionalized alkenes.



Scheme 22. Photocatalytic synthesis of quinoxaline using enaminones and *o*-phenylenediamines.

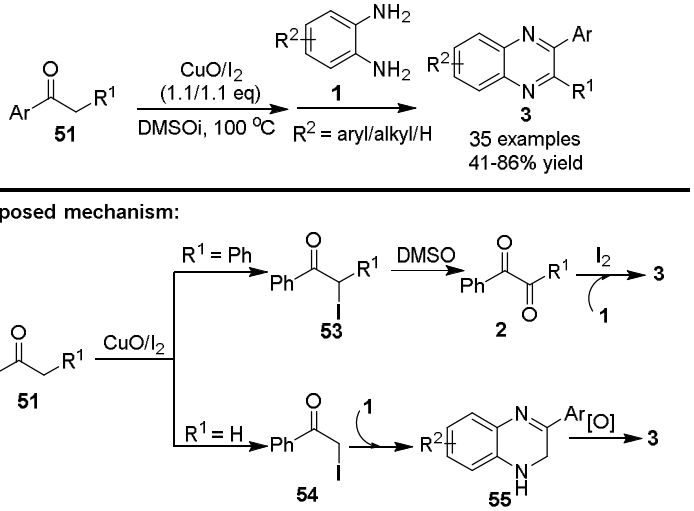
2.5. Reactions with methylene aldehydes and ketones

The methylene C-H bond of ketones and aldehydes are reactive under oxidative condition, the vicinal dicarbonyl intermediate or equivalent species resulted from the oxidation could also be captured by the o-phenylenediamine to yield quinoxalines. Jiang and co-workers[59] developed the DBACO-catalyzed reactions of ketones **51** and *o*-phenylenediamines **1** for the synthesis of 2,3-disubstituted quinoxalines. Under the aerobic atmosphere, the reactions proceeded via the in situ generated vicinal diketone intermediate **2** or the ketone imine intermediate **52** (Scheme 23).



Scheme 23. DBACO-catalyzed synthesis of quinoxalines using methylene ketone.

On the other hand, Wu and Yin[60] et al reported that the reactions of methyl or methylene ketones **51** could take part in the synthesis quinoxalines by reacting with o-phenylenediamine via the promotion of CuO and molecular iodine. As shown in Scheme 24, the reactions of methylene ketones was believed to initiated by the formation of iodinated intermediate **53** and the 1,2-diketone **2** resulted from Kornblum oxidation. And the reactions of equivalent methyl ketone might give corresponding products **3** via the formation of iodoketone **54** and the dihydroquinoxaline **55**.

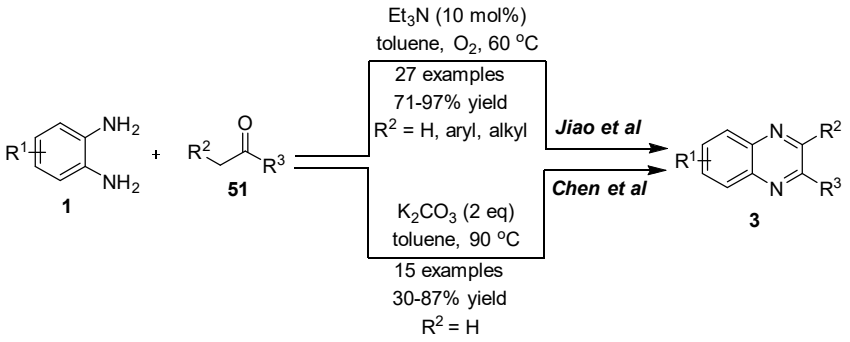


Scheme 24. CuO/I_2 mediated synthesis of quinoxalines using methyl/methylene ketones.

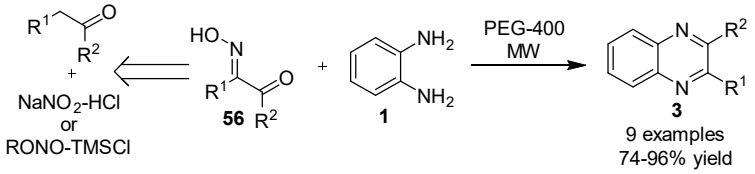
Jiao et al[61] explored and achieved the synthesis quinoxaline by using methylene aldehydes **51** (R^2 = H) and *o*-phenylenediamine via the catalysis of triethyl amine and aerobic oxidation, which enabled the synthesis of 2-substituted products. This catalytic method also tolerated the reactions of methylene ketones ($R^2 \neq$ H) (Scheme 25). On the contrary, Chen and co-workers[62] reported a different catalytic approach employing K_2CO_3 (2 eq) as the base promoter for identical synthesis of 2-substituted quinoxalines using methylene aldehydes and *o*-phenylenediamines (Scheme 25).

2.6. Reactions with other substrates

Alongside the above mentioned reactions partners, there were also other compounds which were found as applicable substrates in the synthesis of quinoxalines by incorporating o-phenylenediamines. Nagendrappa and co-workers[63] reported the synthesis of quinoxaline via the reactions of α-keto oximes **56** and *o*-phenylenediamine via the irradiation of microwave (Scheme 26).

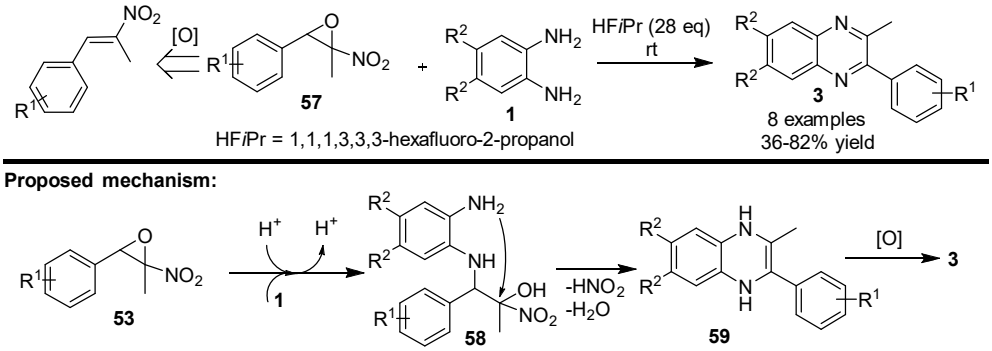


Scheme 25. Synthesis of quinoxalines using methylene ketones/aldehydes.



Scheme 26. Synthesis of quinoxalines usingα-keto oximes and *o*-phenylenediamine.

Tsogoeva et al[64] employed the nitro functionalized epoxides **57** which were generated in situ by the oxidation of the corresponding nitroolefins to couple o-phenylenediamine for the synthesis of quinoxalines. The reactions took place in the presence of 1,1,1,3,3,3-hexafluoro-2-propanol (HF*i*Pr) at room temperature. Species **58** and dihydroquinoxaline **59** were proposed as the key intermediates during the formation of the quinoxaline products (Scheme 27).

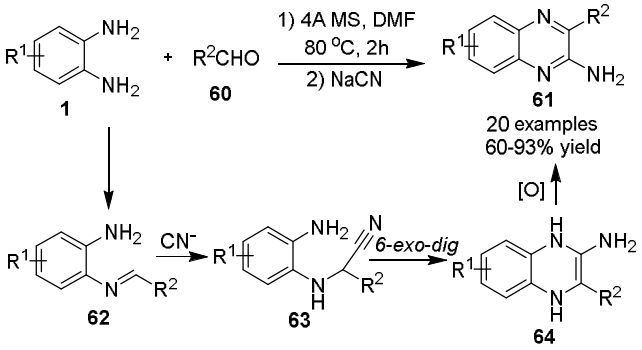


Scheme 27. Synthesis of quinoxalines usingα-nitro epoxides and *o*-phenylenediamine.

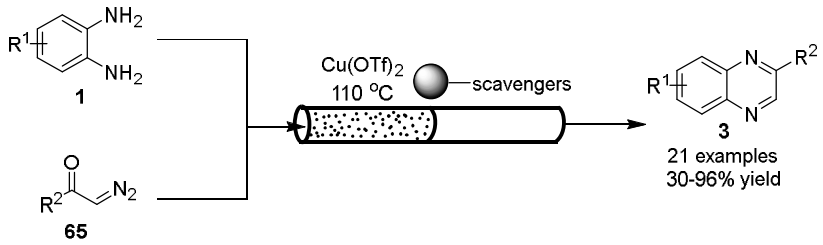
Cheon et al[65] reported a stepwise synthesis of 2-aminoquinoxalines **61** using o-phenylenediamine, aldehyde and sodium cyanide as starting materials. First, the condensation of diamine **1** and aldehyde **60** provided inmine **62**, and the addition of cyano anion to the C=N bond led to the formation of intermediate **63** which underwent selectively *6-exo-dig* cyclization to afford the amino dihydroquinoxaline intermediate **64**. The 2-amino quinoxaline products were finally generated via the oxidation of **64** (Scheme 28).

The synthesis of quinoxalines employing diazoketones as the reaction partners of o-phenylenediamines was realized by Martin and co-workers[66] in the continuous flow reactor. The reactions were conducted by making use of $Cu(OTf)_2$ as the metal catalyst and running through a series of different scavengers including PS-thiourea (polymer supported thiourea, QP-TU), PS-isocyanate (TS-TsNCO)/PS-tosyl chloride (PS-TsCl)

and PS-tosyl hydrazine (PS-TsNHNH$_2$). In operating the reactions, the potentially explosive diazoketiones were generated from acyl chlorides and TMSN$_2$ in another flow line before merging the diamine substrate, and therefore required no addition purification step (Scheme 29).



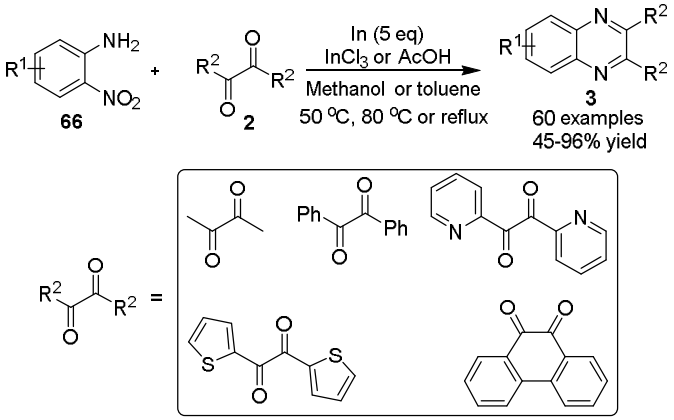
Scheme 28. Quinoxaline synthesis using o-phenylenediamine, aldehyde and sodium cyanide.



Scheme 29. Continuous flow synthesis of quinoxalines using diazoketones and o-phenylenediamines.

3. Synthesis using *o*-nitroanilines as o-phenylenediamine precursors

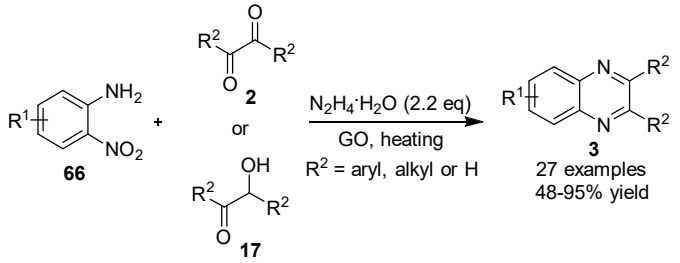
Nitro group is the typical precursor of amino group, the in situ generation of *o*-phenylenediamine from corresponding o-nitroaniline has thus been discovered as applicable strategy in the synthesis of quinoxalines in the presence of proper reaction partners and catalyst. Kim and co-workers[67] reported the synthesis of quinoxalines using o-nitroanilines **66** and vicinal diketone (Scheme 30).



Scheme 30. Synthesis of quinoxalines using o-nitroanilines and vicinal diketones via indium reduction.

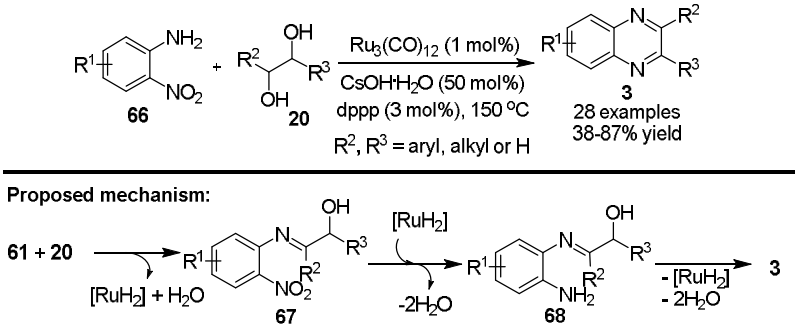
The products **3** were acquired with fair to excellent yields and broad application scope in the presence of elemental indium reductant, and dialkyl, diaryl, diheteroaryl and phenanthrene-9,10-dione were all smoothly tolerated (Scheme 30).

The graphene oxide (GO) was found as practical catalyst to promote the reductive condensation of **66** and vicinal diketones to give quinoxalines, too. As reported by Basu et al,[68] the employment of hydrazine monohydrate as reductant could afford the reduced graphene oxide (rGO) and enabled the formation of quinoxaline products. Notably, besides vicinal diketones, α-hydroxyl diketone **17** was also practical partners of this synthesis (Scheme 31).



Scheme 31. Synthesis of quinoxalines using *o*-nitroanilines and vicinal diketones via hydrazine reduction.

On the other hand, Zhang and co-workers[69] reported an efficient hydrogen transfer strategy for quinoxaline synthesis by employing directly the vicinal diols **20** as the reaction partners of o-nitroanilines. $Ru_3(CO)_{12}$ was employed as the catalyst to enable the expect transformation in the presence of $CsOH{\cdot}H_2O$ and dppp (1,3-bis(diphenylphosphino) propane). As proposed in the report, the cascade reactions started from the dehydrogenative condensation of **66** and **20**, which generated intermediate **67** and $[RuH_2]$. The reduction of the nitro group by $[RuH_2]$ then led to the formation of intermediate **63**, and the further dehydrogenative condensation on **68** then allowed the production of quinoxaline products (Scheme 32).



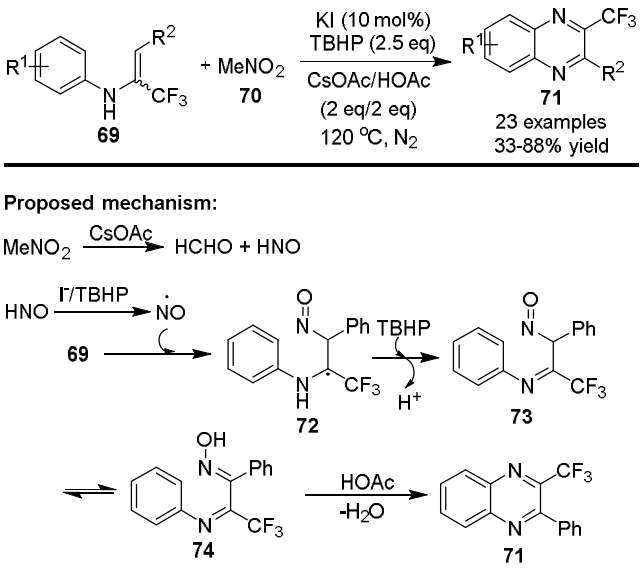
Scheme 32. Synthesis of quinoxalines using *o*-nitroanilines and vicinal diols.

4. Reactions without *o*-phenylenediamine

According to the above introduction, it can be easily seen that the employment of o-phenylenediamines was the predominant strategy in the construction of quinoxaline heterocycle. While high reactivity toward different reaction partners was a favored feature of the *o*-phenylenediamines, these methods were also limited by the hard availability of o-phenylenediamines containing varied substitution, and the formation of mixed region-isomers in many reactions involving substituted *o*-phenylenediamines. Therefore, exploring new substrates which allow flexible variation in substructure is highly crucial in term of the molecular diversity of the quinoxaline.

4.1. Reactions involving aryl C-H functionalization

Zhang et al[70] developed the method on CF_3-functionalized quinoxaline synthesis employing enamines **69** and nitromethane **70** as starting materials. The presence of KI, TBHP, CsOH and AcOH allowed the cascade construction of CF_3-functionalized quinoxalines **71** by heating in $MeNO_2$ at 120 °C. The reactions were proposed to start from the interaction of $MeNO_2$ and CsOH, which yielded HNO as the radical precursor. The decomposition of HNO gave radical NO· by reacting with I⁻/TBHP. The addition of NO· to **69** led to formation of free radical intermediates **72**. The further oxidation of **72** by TBHP afforded nitrone **73** which could present also in the isomeric form **74**. The dehydrative cyclization of **74** then yielded products **71** via the promotion of AcOH (Scheme 33).

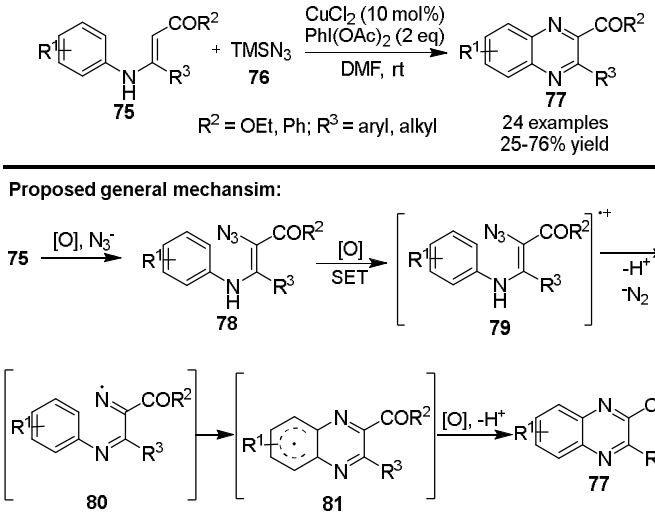


Scheme 33. Cascade reactions of CF_3-based enamine and nitromethane for quinoxaline synthesis.

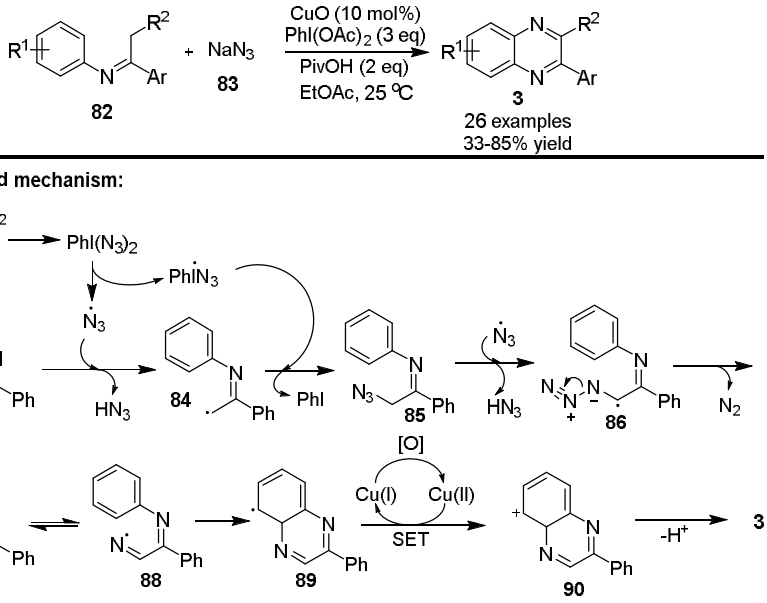
Yu and co-workers[71] established a novel method on the synthesis of acylated quinoxalines **77** via the cascade reactions between enamines **75** and trimethyl silyl azide **76** via $CuCl_2$ catalysis in the presence of $PhI(OAc)_2$. The main transformations of the cascade reactions were proposed as the vinyl C-H azidation providing **78**, the oxidative SET forming radical cation **79**, the nitrogen extrusion and deprotonation giving radical **80**, and the radical cyclization providing **81**. The products were generated from the oxidation of free radical intermediate **81** by losing proton (Scheme 34).

On the other hand, Zeng et al[72] developed the cascade construction of quinoxalines **3** via the reaction of imines **82** and sodium azide **83** via the catalysis of CuO via also the assistance of $PhI(OAc)_2$. In the reactions, it was believed that the generation of azide radical from the in situ generated $PhI(N_3)_2$ initiated the cascade process. The subsequent formation of free radical intermediate **84**, azide species **85**, and radical intermediates **86**-**89** were also key transformations in the reactions. In addition, oxidative SET on **83** enabled the occurrence of the cation **90** which then gave rise to the quinoxaline products by releasing proton (Scheme 35).

Recently, Mo and Su et al[73] reported the synthesis of quinoxalines by directly employing anilines **91** and the β-keto oximes **92** by a two-step protocol involving cascade C-N bonds formation. The tandem operations of AcOH promoted condensation forming **93**, and the formation of quinoxaline cation **95** either by the nucleophilic cyclization of **93** or another cation **94** mediated by $POCl_3$ were possibly the main transformations of the cascade reaction (Scheme 36).



Scheme 34. Cascade reactions of enamine and $TMSN_3$ for quinoxaline synthesis.

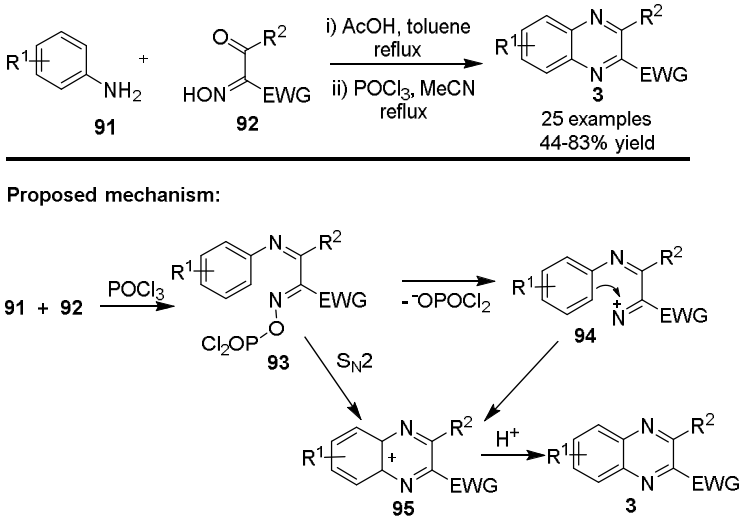


Scheme 35. Cascade reactions of imine and NaN_3 for quinoxaline synthesis.

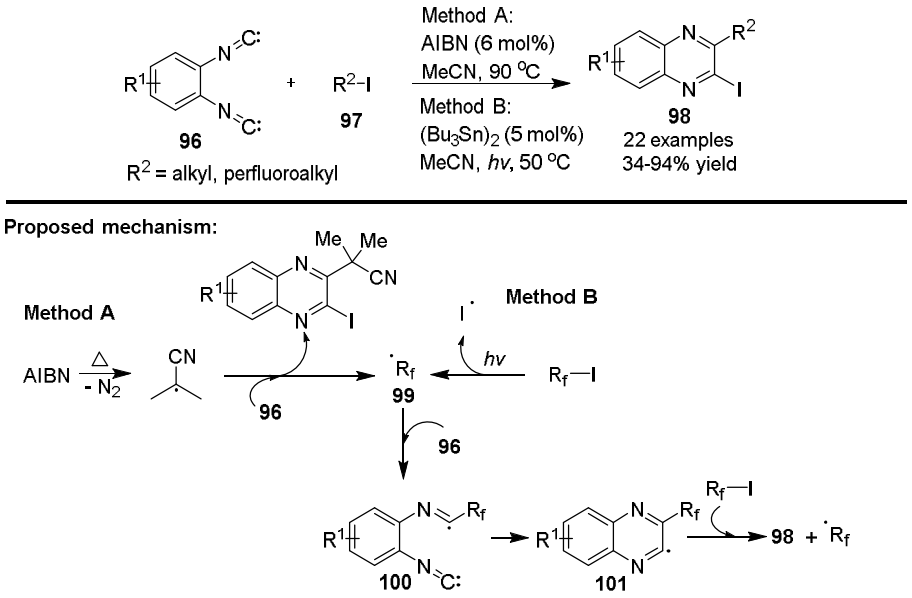
4.2. Reactions using *ortho*-diisocyanoarenes

Early in 1990s, the *ortho*-diisocyanoarenes were employed for the construction of quinoxaline ring in the synthesis of quinoxaline oligomers by reacting with organometal reagents.[74-75] Recently the synthesis of small quinoxalines using such compounds was realized by Studer and Leifert.[76] They reported the synthesis of iodine substituted quinoxalines **98** by the reactions of *ortho*-diisocyanoarenes **96** and perfluoroalkyl/alkyl halides **97** via the catalysis of either AIBN (α,α'-azobisisobutyronitrile) or $(Bu_3Sn)_2$/visible light via the atom transfer radical addition process. The cascade construction was initiated by the generation of perfluoroalkyl radical **99** via the incorporation of AIBN to **96** (method A) or the photo-induced homo-

cleavage of R_f-I bond (method B). The addition of **99** to substrate **96** led to the generation of intermediate **100** which underwent a subsequent intramolecular radical addition to provide **101**. The radical substitution of **101** to the substrate R_f-I then yielded the quinoxaline product **98** (Scheme 37).



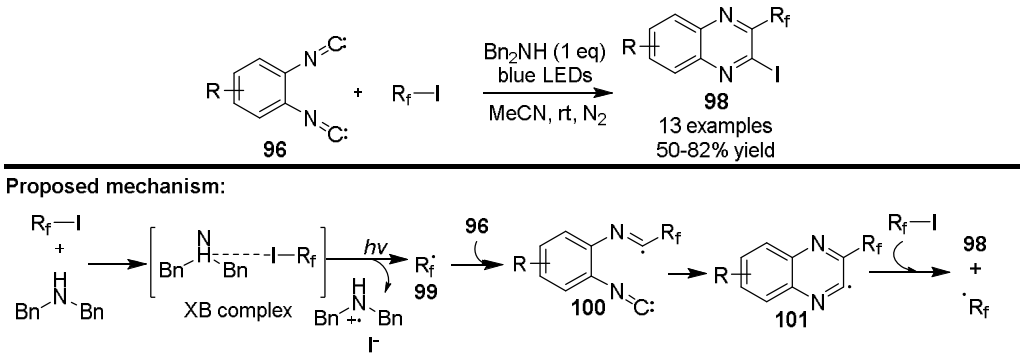
Scheme 36. Cascade reactions of anilines and β-keto oximes for quinoxaline synthesis.



Scheme 37. Synthesis of quinoxalines using *ortho*-diisocyanoarenes and perfluoroalkyl/alkyl iodides.

In the same year, Yu et al[77] reported the same kind of reactions for synthesis perfluoroalkylated quinoxalines **98** via visible light irradiation in the presence of Bn_2NH in MeCN medium. In this catalytic protocol, the interaction between the amine and the iodine atom forming halogen bond (XB) complex was

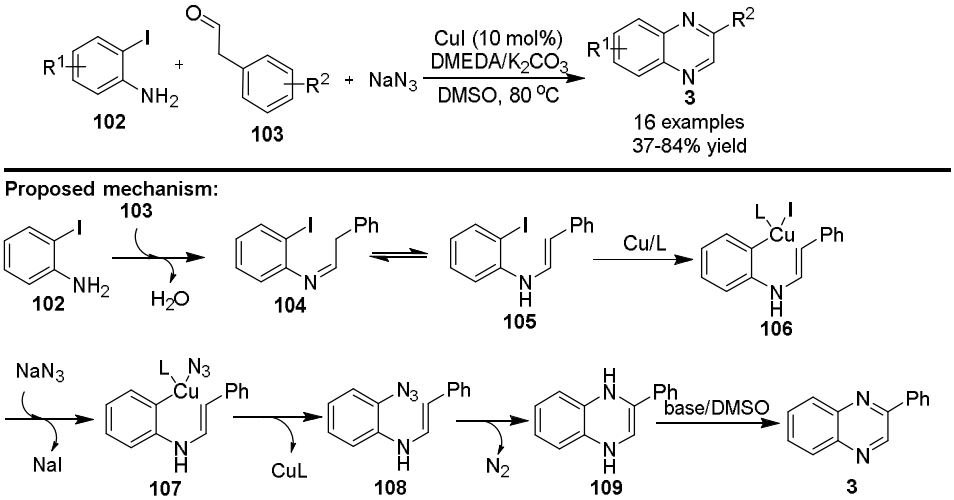
proposed as the key factor which facilitated the generation of perfluoroalkyl radical **99**, which then proceed consequent cascade transformations to provide products **98** via similar process in Studer's work (Scheme 38).



Scheme 38. Amine-mediated synthesis of quinoxalines.

4.3. Other reactions

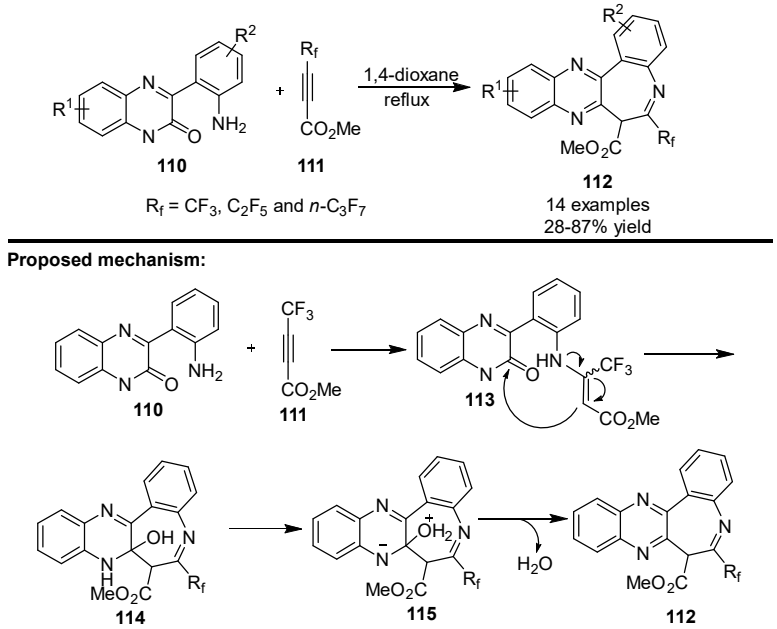
Chen and co-workers[78] reported the synthesis of quinoxalines via copper-catalyzed three-compound cross-coupling reactions using o-iodoanilines **102**, aryl acetaldehydes **103** and sodium azide. The reactions were proposed to proceed from the condensation between **102** and **103**, which gave imine intermediate **104**. Enamine **105**, the isomeric version of **104** incorporated copper catalyst and the ligand by the oxidative addition of the Ar-I bond then proceeded to copper complex **106**, and the following substation of the iodide ion with azide ion afforded **107**. The reductive elimination of this complex yielded aryl azide intermediate **108**. The intramolecular vinyl C-H amination of **108** by a nitrogen extrusion led to the formation of dihydroquinoxaline **109** which underwent the final oxidative aromatization to provide quinoxaline products (Scheme 39).



Scheme 39. Copper-catalyzed cross-coupling cascade synthesis of quinoxalines.

Cao et al[79] recently reported the synthesis of perfluoroalkyl functionalized quinoxalines fused with benzoazepine. By simply refluxing quinoxalinones **110** and perfluoroalkyl functionalized propiolates **111**, the polycyclic quinoxalines **112** were afforded with fair to good yiels. Generally, the reactions involved the

Michael-type addition forming enamine intermediate **113**, the intramolecular nucleophilic addition to the carbon providing hydroxylated compound **114**, and formation of target products via the deprotonated intermediates **115** (Scheme 40).



Scheme 40. Synthesis of ring fused quinoxalines using quinoxalinones.

5. Conclusions

Conclusively, as heterocyclic motif showing widespread application in organic synthesis, materials, and pharmaceutical chemistry etc, quinoxalines have attracted extensive interest as targets of synthetic organic chemistry. Generally, notable advances have taken place in the research area of quinoxaline synthesis over the past decade. As representative methods in quinoxaline construction, the synthetic methods employing o-phenylenediamines as key building blocks have been utilized the mainstream strategy. Efforts in this direction have led to the discoveries of many different reaction partners of o-phenylenediamines which enabled the formation of structurally diverse quinoxaline products. On the other hand, however, the limited availability on the structurally variable o-phenylenediamines as well as the mixed isomeric products in those reactions involving planar asymmetrical *o*-phenylenediamine are the main challenges facing these synthetic protocols. It is fortunate that alternative approaches using simpler substrates such anilines etc have been developed to partially complement those *o*-phenylenediamine-based synthesis, which allowed the synthesis of many quinoxalines with more flexible variation on the substructures of the starting materials, and/or improved product selectivity. While the overall models of o-phenylenediamine-free quinoxaline synthesis are yet scarce, extensive efforts in devising much more different methods on the synthesis of quinoxalines by employing structurally simple and easily available substrates are therefore still highly demanding. In addition, sustainable catalytic methods which are capable of providing quinoxalines with much cleaner operation and lower cost are also highly desirable.

Acknowledgements

Financial supports from National Natural Science Foundation of China (21562025) and Natural Science Foundation of Jiangxi Province (20161ACB21010), and the Science Fund for Distinguished Young Scholars of Jiangxi Province (20162BCB23023) are gratefully acknowledged.

References

1. Xia, Q.-H.; Hu, W.; Li, C.; Wu, J.-F.; Yang, L.; Han, X.-M.; Shen, Y.-M.; Li, Z.-Y.; Li, X. *Eur. J. Med. Chem.* **2016**, *124*, 311-325.
2. Munk, S. A.; Harcourt, D.; Arasasingham, P.; Gluchowski, C.; Wong, H.; Burke, J.; Kharlamb, A.; Manlapaz, C.; Padillo, E.; Williams, L.; Wheeler, L.; Garst, M. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 1745-1750.
3. Kim, Y. B.; Kim, Y. H.; Park, J. Y.; Kim, S. K. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 541-544.
4. Sessler, J. L.; Maeda, H.; Mizuno, F.; Lynch, V. M.; Furuta, H. *J. Am. Chem. Soc.* **2002**, *124*, 13474-13479.
5. Hui, X.; Desrivot, J.; Bories, C.; Loiseau, P. M.; Franck, X.; Hocquemiller, R.; Figadere, B. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 815-820.
6. Brown, D. J. In *The Chemistry of Heterocyclic Compounds, Quinoxalines: Supplement II*; Taylor, E. C.; Wipf, P., Eds.; Wiley: New Jersey, **2004**.
7. More, S. V.; Sastry, M. N. V.; Yao, C.-F. *Green Chem.* **2006**, *8*, 91-95.
8. Ajaikumar, S.; Pandurangan, A. *Appl. Catal. A: Gen.* **2009**, *357*, 184-192.
9. Liu, J.-Y.; Liu, J.; Wang, J.-D.; Jiao, D.-Q.; Liu, H.-W. *Synth. Commun.* **2010**, *40*, 2047-2056.
10. Kumbhar, A.; Kamble, S.; Barge, M.; Rashinkar, G.; Salunkhe, R. *Tetrahedron Lett.* **2012**, *53*, 2756.
11. Kadam, H. K.; Khan, S.; Kunkalkar, R. A.; Tilve, S. G. *Tetrahedron Lett.* **2013**, *54*, 1003-1007.
12. Brahmachari, G.; Laskar, S.; Barik, P. *RSC Adv.* **2013**, *3*, 14245-14253.
13. Baghbanian, S. M. Chin. Chem. Lett. **2015**, *26*, 1113-1116.
14. Zhang, X.-Z.; Wang, J.-X.; Bai, L. *Synth. Commun.* **2011**, *41*, 2053-2063.
15. Narsaiah, A. V.; Kumar, J. K. *Synth. Commun.* **2012**, *42*, 883-892.
16. Delpivo, C.; Micheletti, G.; Boga, C. *Synthesis* **2013**, *45*, 1546-1552.
17. Kumar, D.; Seth, K.; Kommi, D. N.; Bhagat, S.; Chakraborti, A. K. *RSC Adv.* **2013**, *3*, 15157-15168.
18. Lassagne, F.; Chevallier, F.; Roisnel, T.; Dorcet, V.; Mongin, F.; Domingo, L. R. *Synthesis* **2015**, *47*, 2680-2689.
19. Ayaz, M.; Martinez-Ariza, G.; Hulme, C. *Synlett* **2014**, *25*, 1680-1684.
20. Das, B.; Venkateswarlu, K.; Suneel, K.; Majhi, A. *Tetrahedron Lett.* **2007**, *48*, 5371-5374.
21. Wan, J.-P.; Gan, S.-F.; Wu, J.-M.; Pan, Y.-J. *Green Chem.* **2009**, *11*, 1633-1637.
22. Madhav, B.; Murthy, N. M.; Reddy, V. P.; Rao, K. R.; Nageswar, Y. V. D. *Tetrahedron Lett.* **2009**, *50*, 6025-6028.
23. Meshram, H. M.; Ramesh, P.; Kumar, G. S.; Reddy, B. C. *Tetrahedron Lett.* **2010**, *51*, 4313-4316.
24. Ghosh, P.; Mandal, A. *Tetrahedron Lett.* **2012**, *53*, 6483-6488.
25. Kumar, K.; Mudshinge, S. R.; Goyal, S.; Gangar, M.; Nair, V. A. *Tetrahedron Lett.* **2015**, *56*, 1266-1271.
26. Kumar, B. S. P. A.; Madhav, B.; Reddy, K. H. V.; Nageswar, Y. V. D. *Tetrahedron Lett.* **2011**, *52*, 2862-2865.
27. Raw, S. A.; Wilfred, C. D.; Taylor, R. J. K. *Chem. Commun.* **2003**, 2286-2287.
28. Raw, S. A.; Wilfred, C. D.; Taylor, R. J. K. *Org. Biomol. Chem.* **2004**, *2*, 788-796.
29. Kim, S. Y.; Park, K. H.; Chung, Y. K. *Chem. Commun.* **2005**, 1321-1323.
30. Cho, C. S.; Oh, S. G. *J. Mol. Catal. A: Chem.* **2007**, *276*, 205-210.
31. Sithambaram, S.; Ding, Y.; Li, W.; Shen, X.; Gaenzler, F.; Suib, S. L. *Green Chem.* **2008**, *10*, 1029-1032.
32. Akkilagunta, V. K.; Reddy, V. P.; Kakulapati, R. R. *Synlett* **2010**, 2571-2574.
33. Song, W.; Liu, P.; Lei, M.; You, H.; Chen, X.; Chen, H.; Ma, L.; Hu, L. *Synth. Commun.* **2012**, *42*, 236-245.
34. Pan, F.; Chen, T.-M.; Cao, J.-J.; Zou, J.-P.; Zhang, W. *Tetrahedron Lett.* **2012**, *53*, 2508-2510.
35. Kamal, A.; Babu, K. S.; Faazil, S.; Hussaini, S. M. A.; Shaik, A. B. *RSC Adv.* **2014**, *4*, 46369-46377.
36. Shah, N.; Gravel, E.; Jawale, D. V.; Doris, E.; Namboothiri, I. N. N. *ChemCatChem* **2015**, *7*, 57-61.
37. Kamal, A.; Babu, K. S.; Hussaini, S. M. A.; Mahesh, R.; Aldarifi, A. *Tetrahedron Lett.* **2015**, *56*, 2803-2808.
38. Jeena, V.; Sithebe, S.; Robinson, R. S. *Synth. Commun.* **2015**, *45*, 1484-1491.

39. Harsha, K. B.; Rangappa, K. S. *RSC Adv.* **2016**, *6*, 57154-57162.
40. Zhang, Z.; Xie, C.; Feng, L.; Ma, C. *Synth. Commun.* **2016**, *46*, 1507-1518.
41. Cho, C. S.; Oh, S. G. *Tetrahedron Lett.* **2006**, *47*, 5633-5636.
42. Climent, M. J.; Corma, A.; Hernádez, J. C.; Hungría, A. B.; Iborra, S.; Martínez-Silvestre, S. *J. Catal.* **2012**, *292*, 118-129.
43. Mousset, C.; Provot, O.; Hamze, A.; Bignon, J.; Brion, J.-D.; Alami, M. *Tetrahedron* **2008**, *64*, 4287.
44. Chandrasekhar, S.; Kesava, N.; Kumar, R. V. P. *Tetrahedron Lett.* **2010**, *51*, 3623.
45. Shi, S.; Wang, T.; Yang, W.; Rudolph, M.; Hashmi, A. S. K. *Chem. Eur. J.* **2013**, *19*, 6576-6580.
46. Xu, Y.; Wan, X. *Tetrahedron Lett.* **2013**, *54*, 642-645.
47. Chen, C.-Y.; Hu, W.-P.; Liu, M.-C.; Yan, P.-C.; Wang, J.-J.; Chung, M.-I. *Tetrahedron* **2013**, *69*, 9735-9741.
48. Viswanadham, K. K. D. R.; Reddy, M. P.; Sathyanarayana, P.; Ravi, O.; Kant, R.; Bathula, S. R. *Chem. Commun.* **2014**, *50*, 13517-13520.
49. Vadagaonkar, K. S.; Kalmode, H. P.; Murugan, K.; Chaskar, A. C. *RSC Adv.* **2015**, *5*, 5580-5590.
50. Hazarika, D.; Phukan, P. *Tetrahedron* **2017**, *73*, 1374-1379.
51. Okumura, S.; Takeda, Y.; Kiyokawa, K.; Minakata, S. *Chem. Commun.* **2013**, *49*, 9266-9268.
52. Wang, W.; Shen, Y.; Meng, X.; Zhao, M.; Chen, Y.; Chen, B. *Org. Lett.* **2011**, *13*, 4514-4517.
53. Wang, Z.; Hu, G.; Liu, J.; Liu, W.; Zhang, H.; Wang, B. *Chem. Commun.* **2015**, *51*, 5069-5072.
54. Shen, J.; Wang, X.; Lin, X.; Yang, Z.; Cheng, G.; Cui, X. *Org. Lett.* **2016**, *18*, 1378-1381.
55. Chen, Y.; Li, K.; Zhao, M.; Li, Y.; Chen, B. *Tetrahedron Lett.* **2013**, *54*, 1627-1630.
56. Li, C.; Zhang, F.; Yang, Z.; Qi, C. *Tetrahedron Lett.* **2014**, *55*, 5430-5433.
57. Yang, Y.; Ni, F.; Shu, W.-M.; Wu, A.-X. *Chem. Eur. J.* **2014**, *20*, 11776-11782.
58. Cao, S.; Zhong, S.; Xin, L.; Wan, J.-P.; Wen, C. *ChemCatChem* **2015**, *7*, 1478-1482.
59. Qi, C.; Jiang, H.; Huang, L.; Chen, Z.; Chen, H. *Synthesis* **2011**, 387-396.
60. Lian, M.; Li, Q.; Zhu, Y.; Yin, G.; Wu, A. *Tetrahedron* **2012**, *68*, 9598-9605.
61. Zhang, C.; Xu, Z.; Zhang, L.; Jiao, N. *Tetrahedron* **2012**, *68*, 5258-5262.
62. Song, J.; Li, X.; Chen, Y.; Zhao, M.; Dou, Y.; Chen, B. *Synlett* **2012**, *23*, 2416-2420.
63. Padmavathy, K.; Nagendrappa, G.; Geetha, K. V. *Tetrahedron Lett.* **2011**, *52*, 544-547.
64. Ibrahim, M. M.; Grau, D.; Hampel, F.; Tsogoeva, S. B. *Eur. J. Org. Chem.* **2014**, 1401-1405.
65. Cho, Y.-H.; Kim, K.-H.; Cheon, C.-H. *J. Org. Chem.* **2014**, *79*, 901-907.
66. Martin, L. J.; Marzinzik, A. L.; Ley, S. V.; Baxendale, I. R. *Org. Lett.* **2011**, *13*, 320-323.
67. Go, A.; Lee, G.; Kim, J.; Bae, S.; Lee, B. M.; Kim, B. H. *Tetrahedron* **2015**, *71*, 1215-1226.
68. Roy, B.; Ghosh, S.; Ghosh, P.; Basu, B. *Tetrahedron Lett.* **2015**, *56*, 6762-6767.
69. Xie, F.; Zhang, M.; Jiang, H.; Chen, M.; Lv, W.; Zhang, A.; Jian, X. *Green Chem.* **2015**, *17*, 279-284.
70. Yang, Z.-J.; Liu, C.-Z.; Hu, B.-L.; Deng, C.-L.; Zhang, X.-G. *Chem. Commun.* **2014**, *50*, 14554-14557.
71. Ma, H.; Li, D.; Yu, W. *Org. Lett.* **2016**, *18*, 868-871.
72. Chen, T.; Chen, X.; Wei, J.; Lin, D.; Xie, Y.; Zeng, W. *Org. Lett.* **2016**, *18*, 2078-2081.
73. Jiao, Y.-X.; Wu, L.-L.; Zhu, H.-M.; Qin, J.-K.; Pan, C.-X.; Mo, D.-L.; Su, G.-F. *J. Org. Chem.* **2017**, *82*, 4407-4414.
74. Ito, Y.; Ihara, E.; Hirai, M.; Ohsaki, H.; Ohnishi, A.; Murakami, M. *J. Chem. Soc., Chem. Commun.* **1990**, 403-405.
75. Ito, Y.; Ihara, E.; Murakami, M.; Shiro, M. *J. Am. Chem. Soc.* **1990**, *112*, 6446-6447.
76. Leifert, D.; Studer, A. *Angew. Chem. Int. Ed.* **2016**, *55*, 11660-11663.
77. Sun, X.; Wang, W.; Li, Y.; Ma, J.; Yu, S. *Org. Lett.* **2016**, *18*, 4638-4641.
78. Yuan, H.; Li, K.; Chen, Y.; Wang, Y.; Cui, J.; Chen, B. *Synlett* **2013**, *24*, 2315-2319.
79. Liu, G.; Sun, X.; Chen, L.; Wu, Y.; Han, J.; Chen, J.; Deng, H.; Shao, M.; Zhang, H.; Cao, W. *RSC Adv.* **2016**, *6*, 108154-108157.