Check for updates

Accepted Article

Article Type: Full Paper

Using calcium carbide as an acetylene source for cascade synthesis of pyrrolo[2,3-*b*]quinoxalines via copper-free Sonogashira coupling reaction

Mahsa Fakharian[a], Ali Keivanloo,*[a] Mohammad Reza Nabid[b]

[a]*Faculty of Chemistry, Shahrood University of Technology, Shahrood 36199-95161, Iran.*

[b]*Department of Chemistry and Petroleum Faculty of Sciences, Shahid Beheshti University, Evin, Tehran, Iran.*

E-mail addresses: akeivanloo@yahoo.com; keivanloo@shahroodut.ac.ir

Abstract

A palladium-catalyzed cascade protocol has been established for the synthesis of pyrrolo[2,3-b]quinoxalin-2-yl)-4-methylcyclohexanols and pyrrolo[2,3-b]quinoxalin-2-yl)-2-phenylpropan-1-ols through the reaction of *N*-alkyl(aryl)-3-chloroquinoxaline-2-amines with calcium carbide and cyclohexanones or 2-phenylpropanal. This one-pot process, carried out without any copper salt in the key step of the Sonogashira coupling reaction, provides an efficient method for the synthesis of 2,3-disubstituted pyrrolo[2,3-*b*]quinoxalines in the presence of catalytic amounts of $Pd(PPh_3)_2Cl_2$ in DMSO/H_2O with high yields. The benefit of this strategy is the use of a commercially available, inexpensive, and less hazardous primary chemical feedstock, calcium carbide, as an acetylene source in a wet solvent.

Keywords: Calcium carbide, Pyrrolo[2,3-*b*]quinoxalines, Copper-free, Sonogashira coupling.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/hlca.201800004
This article is protected by copyright. All rights reserved.

Accepted Article

Introduction

The chemistry of carbon-carbon triple bonds has been a permanent source of fundamentally important processes and technologies.[1] Acetylene is one of the primary building blocks in synthetic organic and industrial chemistry. It has been the main industrial source of vinyl chloride, acrylonitrile, vinyl acetate, acetaldehyde, and several other important compounds for many decades. Calcium carbide has a number of advantages over acetylene gas. Neither oil nor natural gas is required to synthesize calcium carbide, its transportation does not have the same risks as for acetylene, there is no need to use complicated high-pressure equipment, and working with calcium carbide is safer and more convenient.[2] Furthermore, the use of calcium carbide in organic synthesis is more cost-efficient and safer than the use of acetylene gas. The use of calcium carbide in the presence of palladium catalyst is an efficient protocol for the synthesis of various functional acetylene derivatives. However, its low solubility in almost all solvents and the difficulty in controlling mono-substitution reactions are the major challenges in the direct synthesis of functionalized acetylene derivatives from CaC_2. Cheng and co-workers have reported the synthesis of symmetric diarylethynes from aryl bromides using CaC_2.[3] This strategy was successfully applied for the synthesis of enaminones and propargylic amines through the three-component coupling reaction of CaC_2, aryl aldehydes, and amines [4] as well as a convenient method for the preparation of propargyl alcohols by reacting CaC_2 with aldehydes and ketones in the presence of 50 mol% of cesium carbonate in aqueous DMSO at 60 °C.[5] Novel protocols have already been developed for the synthesis of various functional molecules such as propargylamines,[6] diarylethynes,[7] triazoles,[8] and enaminones [9] from calcium carbide. The use of ethynylmagnesium bromide has also been reported recently as a commercial acetylene surrogate in the Kumada-Negishi-type coupling reactions.[10,11] It was further demonstrated in these protocols that, unlike the traditional methods, multiple

This article is protected by copyright. All rights reserved.

protection and de-protection steps could be avoided with the direct usage of calcium carbide. This greatly reduced the number of synthetic steps, resulting in a more efficient and greener organic synthesis.

The Sonogashira reaction is an important process that is most widely used for the C(sp^2)-C(sp) bond-formation reactions in organic synthesis.[12] It provides an efficient method for the synthesis of aryl alkynes, which are interesting intermediates for the preparation of a variety of target compounds with applications ranging from natural products [13] and pharmaceuticals [14] to molecular organic materials.[15] In the Sonogashira coupling reaction, addition of a catalytic amount of copper(I) iodide, as a co-catalyst, greatly accelerates the reaction, thus enabling the performance of alkynylation at room temperature.[16] The addition of copper salts in the typical Sonogashira coupling reactions also have drawbacks such as being environmentally unfriendly and difficult to recover reagent, and the *in situ* generation of copper acetylides under the reaction conditions often generates homo-coupling products of the terminal alkyne (Glaser coupling).[17] This side-reaction is especially problematic when the terminal acetylene is difficult to obtain or expensive and usually difficult to separate from the desired products,[18] and it has been shown that the presence of a reductive atmosphere formed by difficult-to-handle hydrogen can diminish homocoupling [19] as well as the slow addition of the acetylene.[20] In the recent years, a significant modification has been reported for the Sonogashira coupling procedure, [21-24] and efficient copper-free reactions have been developed.[25-27] These copper-free methodologies are usually called the copper-free Sonogashira coupling reactions. Although copper-free Sonogashira coupling reactions of terminal alkynes with aryl iodides have been widely investigated, few examples with aryl chlorides [28–30] and heteroaryl chlorides [31-33] have been reported.

Multi-component reactions (MCRs) are one-pot reactions in which three or more starting materials react sequentially in a single operation to form a single product, where basically all

This article is protected by copyright. All rights reserved.

Accepted Article

or most of the atoms of the starting materials contribute to the final product formed. In the last decade, transition metals have been widely used for catalysis of new MCRs. Expectedly, palladium-catalyzed processes have received a dominant position; yet, other transition metal complexes such as the rhodium, ruthenium, and copper ones are catching up, implying organometallic elementary steps that reach even further than the cross-coupling and carbometallation reactions.[34-36]

Pyrroloquinoxalines have been extensively studied as bioactive compounds, and many of them are known to be biologically and medicinally useful molecules such as anti-HIV agents, anti-malarial agents, antagonist agents, anti-cancer agents, and PARP-1 inhibitors.[37] Recently, we have reported the synthesis of pyrrolo[2,3-b]quinoxaline derivatives by the Sonogashira coupling reaction of *N*-alkyl-3-chloroquinoxaline-2-amines with terminal alkynes,[38] propargyl bromide,[39] and propargyl alcohols,[40] followed by the subsequent cyclization in a one-pot process. In this work, we attempted to make this overall approach more attractive synthetically using calcium carbide as an acetylene source for the preparation of pyrrolo[2,3-b]quinoxalines.

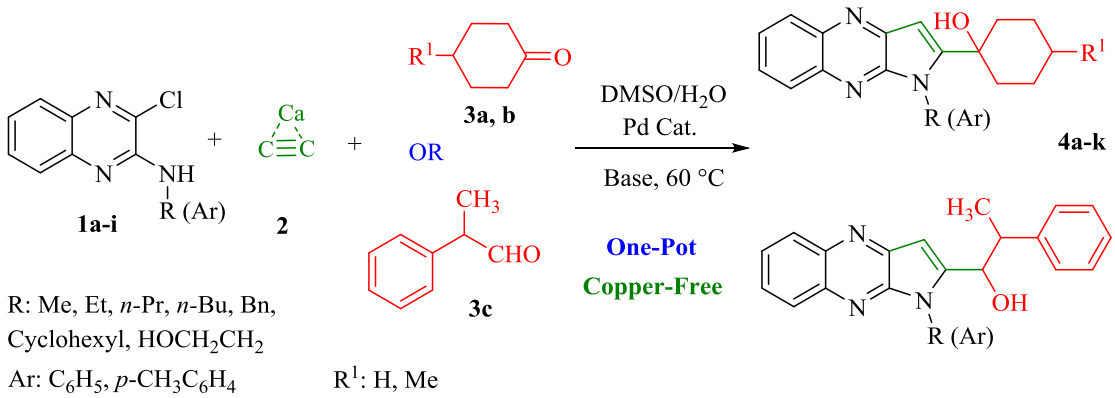
Result and discussion

In continuation of our group's efforts on the application of palladium catalyst for the synthesis of heterocyclic compounds,[41] we have recently used calcium carbide (CaC_2) as a commercially available, low-cost feedstock, safe, and inexpensive reagent for the synthesis of quinoxaline chalcones.[42] In the present work, we wish to report the use of CaC_2 for the synthesis of new 1,2-disubstituted pyrrolo[2,3-*b*]quinoxalines. A cascade palladium-catalyzed reaction of *N*-alkyl(aryl)-3-chloroquinoxaline-2-amines **1a-i**, calcium carbide **2**, and carbonyl compounds **(3a-c)** in DMSO/H_2O afforded pyrrolo[2,3-*b*]quinoxalines substituted by cyclohexanol or phenylpropan-1-ol at position 2 with high yields (Scheme1).

This article is protected by copyright. All rights reserved.

Accepted Article

Scheme 1: One-pot synthesis of 1,2-disubstituted pyrrolo[2,3-*b*]quinoxalines from *N*-alkyl(aryl)-3-chloroquinoxaline-2-amines (**1**), calcium carbide (**2**), and cyclohexanones (**3a**, **b**) or 2-phenylpropionaldehyde (**3c**).



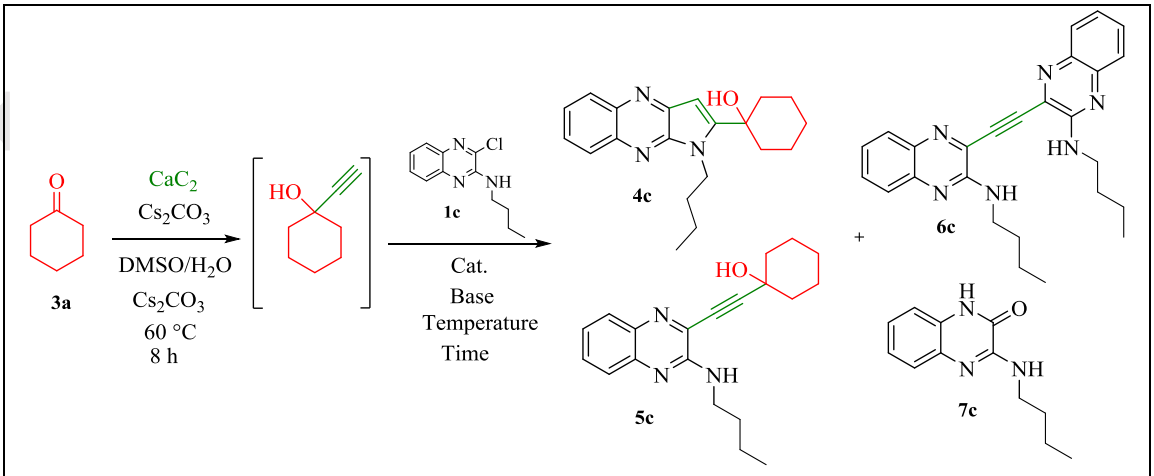
In 2013, Zhang and co-workers,[5] reported the synthesis of terminal acetylenic alcohols from calcium carbide and a restricted number of ketones or aldehydes. According to this work, the best conditions for the preparation of acetylenic alcohols were 2.5 *eqiv*. CaC_2, 1 *eqiv.* aldehyde or ketone, and 0.05 *eqiv.* Cs_2CO_3 in 2 vol% DMSO/H_2O at 60 °C. We used this protocol for the synthesis of 1,2-disubstituted pyrrolo[2,3-*b*]quinoxalines through palladium-catalyzed cascade reactions. In order to optimize the reaction conditions, the reaction of cyclohexanone (**3a**), calcium carbide (**2**) and *N*-butyl-3-chloroquinoxalin-2-amine (**1c**) was used as a model reaction. The investigation, aimed at finding suitable conditions for this cascade transformation, was carried out by the reaction with different bases, catalysts, temperatures, and reaction times in the second step of the reaction. Studies were conducted using different bases including Cs_2CO_3, K_2CO_3, Et_3N, and morpholine for the Sonogashira reaction/heteroannulation. It was found that the organic bases were more suitable than the inorganic ones, and that triethylamine was the most effective base (Table 1, entry 2). Also we studied several palladium catalysts such as $Pd(PPh_3)_2Cl_2$, $Pd(OAc)_2$, $Pd(dba)_2$, and Pd/C in the presence and absence of copper salt. We observed that

This article is protected by copyright. All rights reserved.

Accepted Article

two side-reactions occurred in the presence of copper(I) iodide: one, homo-coupling reaction of copper acetylide with *N*-butyl-3-chloroquinoxaline-2-amine **1c** to afford bisheteroarylethyne **6c** and the other, hydrolysis of chloroquinoxalineamine **1c** to 3-(buthylamino)quinoxalin-2(1*H*)-one (**7c)**. The use of inorganic bases or copper(I) salt increased the hydrolyzed side-product **7ac** (Table 1, entries 13-16). According to the optimization table, $Pd(PPh_3)_2Cl_2$ was the best catalytic system, and afforded the desired product **4c** with a high reaction yield (85%) (Table 1, entry 2). The product formed also depended upon the reaction time. It is noteworthy that the uncyclized compound **5c** was isolated as a major product in low reaction times (2-3 h) (Table 1, entries 7 and 9). Apparently, **5c** is an intermediate of this reaction. The cyclized product **4c** was formed as a major product in a prolonged reaction time; after 6-8 h, it was the sole product (Table 1, entry 7). The suitable reaction temperature was 60 °C; increasing the reaction temperature to 80 °C did not increase the reaction yield (Table 1, entry 8).

Table 1: Optimization reaction conditions for synthesis of 1,2-disubstituted pyrrolo[2,3-*b*]quinoxalines from cyclohexanone **3a**, calcium carbide **2**, and *N*-butyl-3-chloroquinoxalin-2-amine **1c**.[a]



Entry	Base	Catalyst	Time (h)	T (°C)	Yield (%)			
					4c	**5c**	**6c**	**7c**

This article is protected by copyright. All rights reserved.

1	Et_3N	$Pd(PPh_3)_2Cl_2$/CuI	6	60	40	-	40	-
2	Et_3N	$Pd(PPh_3)_2Cl_2$	6	60	85	-	-	-
3	Et_3N	$Pd(PPh_3)_2Cl_2$	3	60	20	70	-	-
4	Et_3N	$Pd(OAc)_2$	6	60	60	10	-	-
5	Et_3N	Pd/C	6	60	30	20	-	-
6	Et_3N	$Pd(dba)_2$	6	60	50	20	-	-
7	Et_3N	$Pd(PPh_3)_2Cl_2$	6	80	80	-	-	-
8	DIPEA	$Pd(PPh_3)_2Cl_2$	6	60	75	-	-	-
9	DIPEA	$Pd(PPh_3)_2Cl_2$/CuI	6	60	40	-	30	-
10	DIPEA	$Pd(PPh_3)_2Cl_2$	3	60	10	75	-	-
11	Morpholine	$Pd(PPh_3)_2Cl_2$	6	60	60	-	-	-
12	Morpholine	$Pd(PPh_3)_2Cl_2$	3	60	40	20	-	-
13	Cs_2CO_3	$Pd(PPh_3)_2Cl_2$	6	60	30	-	-	45
14	Cs_2CO_3	$Pd(PPh_3)_2Cl_2$/CuI	6	60	15	-	30	40
15	K_2CO_3	$Pd(PPh_3)_2Cl_2$	6	60	25	-	-	50
16	K_2CO_3	$Pd(PPh_3)_2Cl_2$/CuI	6	80	15	-	35	30

[a]Reaction conditions: cyclohexanone (1 mmol), Cs_2CO_3 (0.5 mmol), calcium carbide (2.5 mmol) DMSO/H_2O (50:1 mL), at 60 °C, 8 h; and then adding **1a** (0.5 mmol), catalyst (0.05 mmol), base (3.0 mmol), reaction time (h), reaction temperature (°C).

With the optimized reaction conditions in hand, we looked into expanding the substrate scope of this reaction system. In the first step of the reaction, only a few number of aldehydes and ketones were effective. Straight-chain aldehydes, cyclopentanone, and aromatic aldehydes and ketones failed to give the desired product. In 2015, Seidel and Schreiner reported a simple method for the ethynylation of aldehydes and ketones by

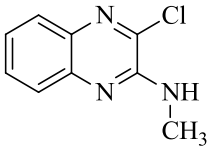
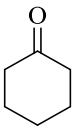
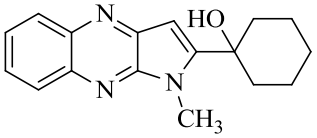
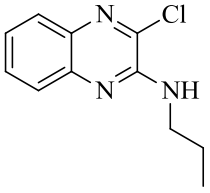
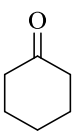
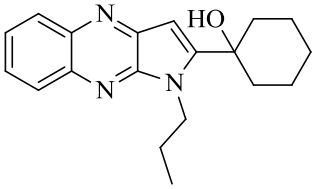
This article is protected by copyright. All rights reserved.

Accepted Article

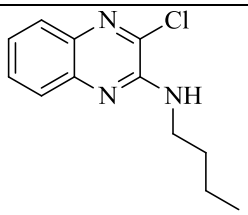
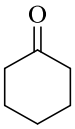
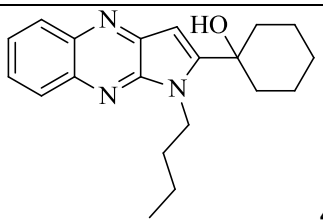
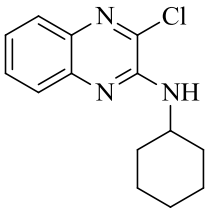
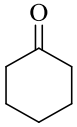
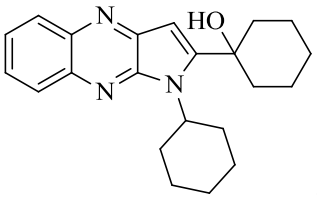
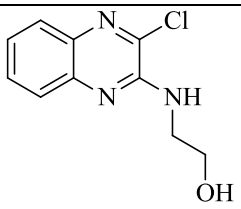
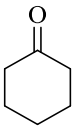
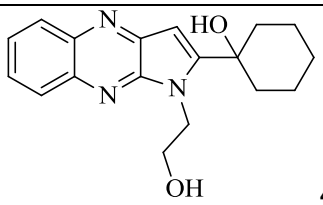
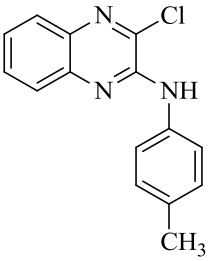
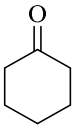
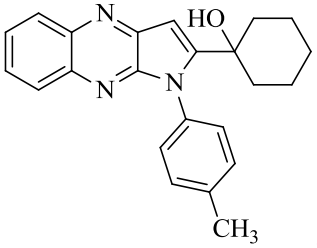
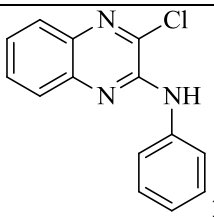
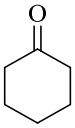
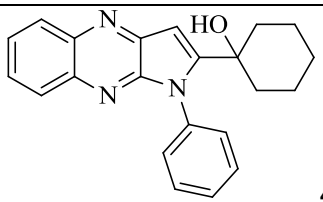
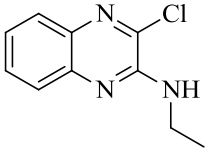
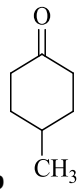
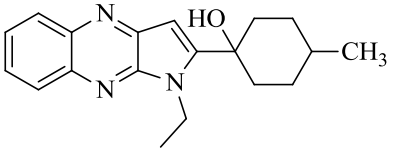
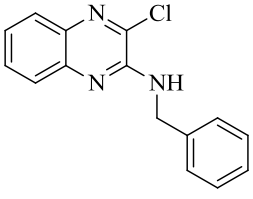
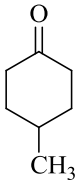
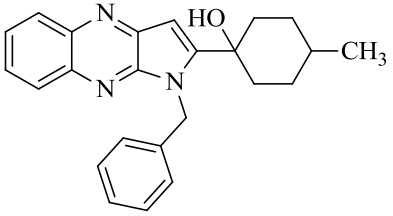
fluoride-assisted activation of calcium carbide. In this method, the reaction of water with solid calcium carbide gives ethynylcalcium hydroxide, which is activated by fluoride from TBAF·$3H_2O$ to form the corresponding ate-complex that attacks the carbonyl compounds.[43] In this article, the restrictions of procedure due to the aldol condensation of carbonyl compounds in the basic medium or steric and torsional strains have been explained. A pK_a value of 26.4 for the carbonyl component was considered as a lower limit to avoid an aldol condensation.[43]

After obtaining the best reaction conditions for the Sonogashira coupling/heteroannulation step, we enhanced a facile cascade procedure for the synthesis of 1,2-disubstituted pyrrolo[2,3-*b*]quinoxalines by the three component reaction of *N*-alkyl(aryl)-3-chloroquinoxaline-2-amines (**1a-i**), calcium carbide (**2**), and cyclohexanone derivatives (**3a,b**) or 2-phenylpropanal (**3c**) in the presence of $Pd(PPh_3)_2Cl_2$ as the catalyst. The results obtained are shown in Table 2.

Table 2: One-pot synthesis of 1,2-dsubstituted pyrrolo[2,3-*b*]quinoxalines from reaction of *N*-alkyl(aryl)-3-chloroquinoxaline-2-amine, calcium carbide, and carbonyl compounds.[a]

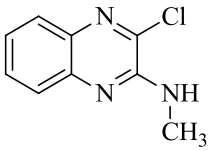
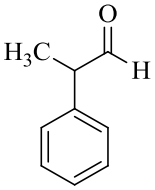
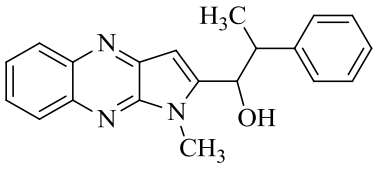
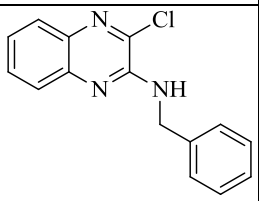
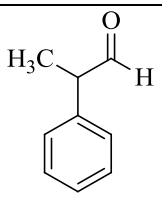
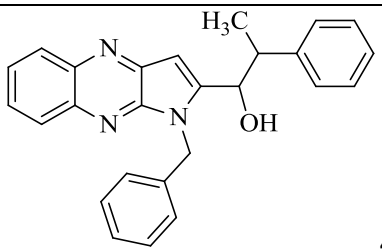
Entry	Quinoxaline amine	Carbonyl compound	Product	Yield (%)
1	 **1a**	 **3a**	 **4a**	85
2	 **1b**	 **3b**	 **4b**	85

This article is protected by copyright. All rights reserved.

3	 **1c**	 **3a**	 **4c**	70
4	 **1d**	 **3a**	 **4d**	85
5	 **1e**	 **3a**	 **4e**	85
7	 **1f**	 **3a**	 **4f**	84
8	 **1g**	 **3a**	 **4g**	75
9	 **1h**	 **3b**	 **4h**	75
10	 **1i**	 **3b**	 **4i**	78

Accepted Article

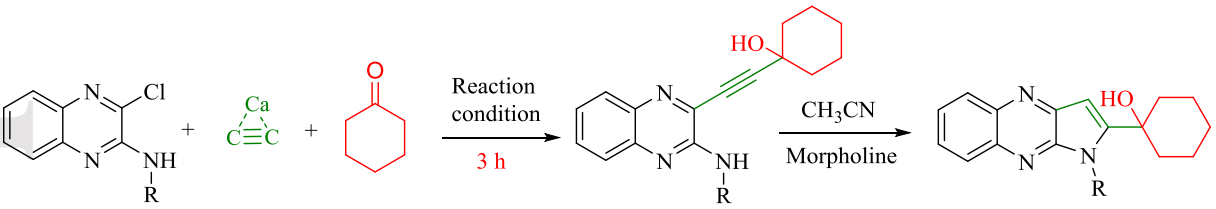
This article is protected by copyright. All rights reserved.

11	 **1a**	 **3c**	 **4j**	70
12	 **1i**	 **3c**	 **4k**	70

[a]Reaction conditions: Cyclohexanone (1 mmol), Cs_2CO_3 (0.5mmol), calcium carbide (2.5 mmol), DMSO/H_2O (50:1 mL), at 60 °C, 8 h; and then adding **1a** (0.5 mmol), catalyst (0.05 mmol), Et_3N (3.0 mmol), reaction time (6-8 h), reaction temperature (60 °C).

The coupling intermediates **5a** and **5b** were formed as major products in a stepwise reaction manner in low reaction times (2-3 h). When these intermediates were slowly warmed in CH_3CN in the presence of morpholine, used as a base, cyclization occurred, and the final products **4a** and **4b** were formed in excellent yields (Scheme 3).

Scheme 3: Synthesis of coupling intermediates 1-((3-(alkylamino)quinoxalin-2-yl)ethynyl)cyclohexanols **5** and their cyclization to pyrrolo[2,3-*b*]quinoxalines **4**.



The structural assignments of the products were based upon the NMR spectroscopic and mass analysis data. The ^1H NMR spectrum of **4c** exhibited two multiplets for the four aromatic protons of the quinoxaline ring at δ 8.10-8.18 and 7.60-7.70, respectively. An aromatic proton at δ 6.38 was characteristic of the fused pyrrole ring. In the aliphatic region, the triplet at δ 4.62 is due to the methylene protons of the butyl

This article is protected by copyright. All rights reserved.

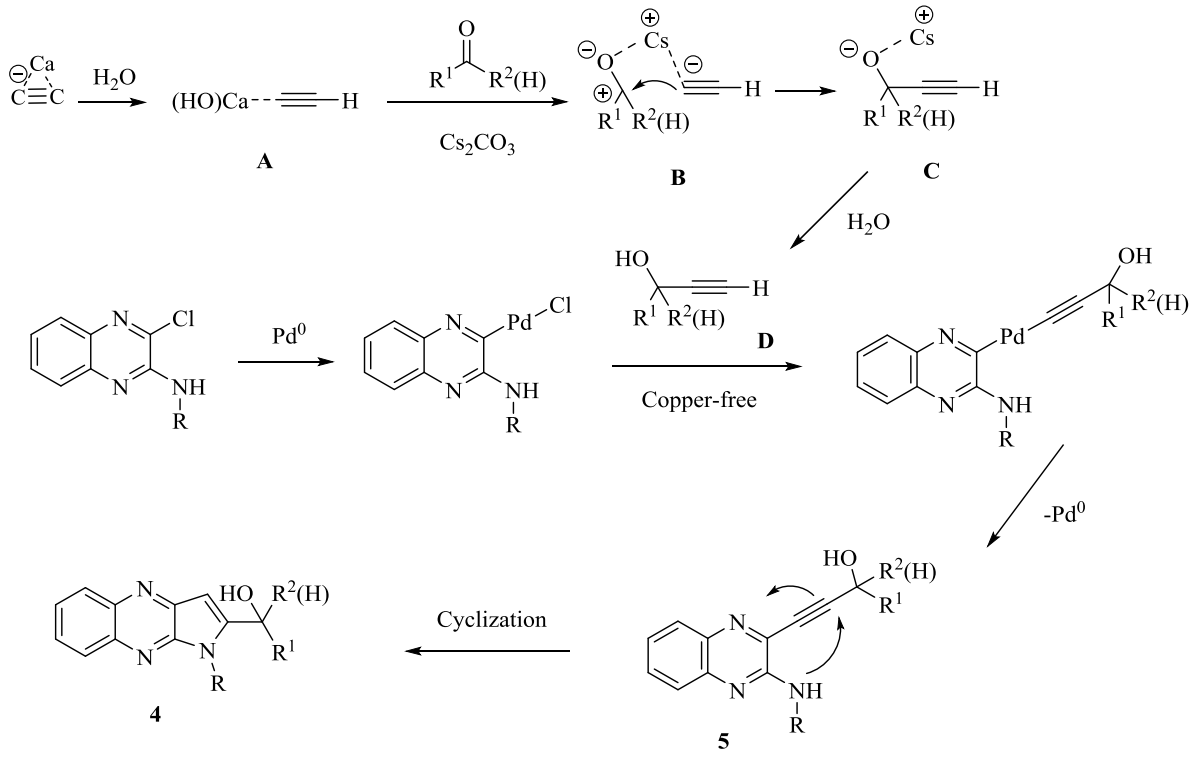
Accepted Article

group. The singlet at δ 2.88 was assigned to the hydroxyl group proton. The multiplets at δ 1.43-2.20 are due to the other seven methylene protons of the butyl and cyclohexyl groups. The triplet at δ 0.97 is due to the methyl protons of the butyl group. The ^{13}C NMR spectrum for this compound showed 18 peaks for the carbon atoms. The mass spectrometer used recorded the molecular ion peak at [M+H] 324 for this compound.

The acetylide ion in calcium carbide (C_2^{2-}) contains two nucleophilic carbons, which, in principle, may react with two carbonyl molecules. However, propargyl alcohols with a terminal alkynyl proton were formed exclusively, and no disubstituted acetylenes were observed. A possible reaction mechanism probably includes the following steps, proposed for the formation of propargyl alcohols from CaC_2.[5] The trace amount of water promotes the reaction by breaking down the polymeric structure of calcium carbide to form calcium acetylide **A**. The presence of base could stabilize the acetylide intermediate and prevent the formation of acetylene. The cesium cation then activates the aldehyde or ketone, and induces a nucleophilic attack of acetylide **A** on the carbonyl group to afford alkoxide **C** via intermediate **B**. Propargyl alcohol **D** is formed by hydrolysis of **C**. In continuation, a copper-free cross-coupling reaction takes place between heteroaryl **1** and propargyl alcohol **D** to afford intermediate **5**. Finally, ring closure by hydroamination/cyclization leads to the formation of 2-substituted pyrrolo[2,3-*b*]quinoxalines **4** (Scheme 3).

This article is protected by copyright. All rights reserved.

Scheme 3. Proposed mechanism for formation of 1,2-disubstituted pyrrolo[2,3-*b*]quinoxalines.



Conclusion

We have developed a practical and efficient strategy for the synthesis of pyrrolo[2,3-*b*]quinoxalines by the reaction of *N*-alkyl(aryl)-3-chloroquinoxaline-2-amines with calcium carbide and cyclohexanones or 2-phenylpropanal under mild conditions. This one-pot cascade reaction was carried out in the presence of catalytic amounts of $Pd(PPh_3)_2Cl_2$ in DMSO/H_2O without any copper salt. The benefit of this strategy is the use of commercially available calcium carbide, as an acetylene source, in a wet solvent.

General information

Melting points were recorded on a Thermocouple digital melting point apparatus. IR spectra were recorded on a Shimadzu IR-435 grating spectrophotometer. For column

This article is protected by copyright. All rights reserved.

Accepted Article

chromatography, Merck Kieselgel 100 was used as the stationary phase. NMR spectra were obtained as $CDCl_3$ solutions using a Bruker 400 and 300 MHz NMR spectrometer. ^1H NMR signals were reported relative to Me_4Si (δ 0.0) or residual $CHCl_3$ (δ 7.26). ^{13}C NMR signals were reported relative to $CDCl_3$ (δ 77.16). Multiplicities were described using the following abbreviations: s = singlet, d = doublet, t = triplet, and m = multiplet. Mass spectra were recorded using a 5975C spectrometer supplied from Agilent Technologies Company.

Typical experimental procedure for synthesis of 2,3-disubstituted pyrrolo[2,3-*b*]quinoxalines (4)

The mixture of a ketone or aldehyde (1 mmol), Cs_2CO_3 (0.5 mmol), calcium carbide (2.5 mmol), and DMSO/H_2O (5:0.1 mL) was stirred at 60 ºC for 8 h. After completion of the reaction (monitored by TLC) an *N*-alkyl(Aryl)-3-chloroquinoxaline-2-amine (0.5 mmol), $Pd(PPh_3)_2Cl_2$ (0.05 mmol), and triethylamine (3.0 mmol) were added, respectively. Stirring the reaction mixture was continued for another 6-8 h at 60 ºC. After completion of the reaction (monitored by TLC), the solvent was evaporated, and the remaining solid was washed with H_2O and then dried. The crude product was purified by column chromatography (silica gel 100) using *n*-hexane/ethyl acetate (80/20).

1-(1-methyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)cyclohexanol (4a)

yellow solid; mp, 193-195 ºC; ^1H NMR (300 MHz, $CDCl_3$): δ 1.54-1.92 (m, 8H, $4CH_2$), 2.08-2.11 (m, 2H, CH_2), 3.34 (s, 1H, OH), 4.12 (s, 3H, CH_3), 6.29 (s, 1H, CH of pyrrole), 7.55-7.64 (m, 2H, 2CH of quinoxaline), 8.06-8.12 (m, 2H, 2CH of quinoxaline); ^{13}C NMR (75 MHz, $CDCl_3$): 21.5, 25.4, 30.8, 36.8, 70.9, 96.4, 126.3, 127.3, 128.1, 128.5, 128.5, 139.2, 140.3, 142.1, 158.1; IR (KBr): 3407, 2944, 2864, 1574, 1523, 1420, 1337, 1177, 966, 761

This article is protected by copyright. All rights reserved.

cm^{-1}; m/z [M+H], 282. Anal. Calcd. for $C_{17}H_{19}N_3O$: C, 72.57; H, 6.81; N, 14.94; Found: C, 72.50; H, 6.84; N, 14.98.

1-(1-propyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)cyclohexanol (4b)

Yellow solid; mp, 140-142 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.98 (t, J = 7.4 Hz, 3H, $NCH_2CH_2CH_3$), 1.57-1.64 (m, 4H, CH_2), 1.82-1.97 (m, 6H, CH_2), 2.08-2.11 (m, 2H, $NCH_2CH_2CH_3$), 4.56 (t, J = 7.7 Hz, 2H, $NCH_2CH_2CH_3$), 5.46 (s, 1H, OH), 6.62 (s, 1H, CH of pyrrole), 7.66-7.72 (m, 2H, 2CH of quinoxaline), 8.07-8.12 (m, 2H, 2CH of quinoxaline); ^{13}C NMR (75 MHz, DMSO-d_6): 11.8, 12.6, 22.9, 25.6, 37.3, 46.1, 70.9, 96.2, 126.6, 127.6, 128.5, 129.0, 138.8, 140.6, 142.8, 143.3, 160.5; IR (KBr): 3317, 2956, 2932, 1582, 1532, 1465, 1414, 1096, 755 cm^{-1}; m/z [M+H], 310. Anal. Calcd. for $C_{19}H_{23}N_3O$: C, 73.76; H, 7.49; N, 13.58; Found: C, 73.79; H, 7.74; N, 13.59.

1-(1-butyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)cyclohexanol (4c)

Yellow solid; mp, 113-115 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.97 (t, J = 7.4 Hz, 3H, $NCH_2CH_2CH_2CH_3$), 1.43-1.55 (m, 2H, CH_2), 1.58-1.79 (m, 4H, $2CH_2$), 1.82-1.93 (m, 6H, $3CH_2$), 2.08-2.20 (m, 2H, CH_2), 2.88 (s, 1H, OH), 4.62 (t, J = 7.9 Hz, 2H, $NCH_2CH_2CH_2CH_3$), 6.38 (s, 1H, CH of pyrrole), 7.61-7.68 (m, 2H, 2CH of quinoxaline), 8.11-8.17 (m, 2H, 2CH of quinoxaline); ^{13}C NMR (75 MHz, $CDCl_3$): 13.8, 20.3, 21.5, 25.3, 31.9, 37.3, 44.5, 71.0, 96.4, 126.3, 127.1, 128.5, 130.5, 139.3, 140.3, 142.2, 143.6, 158.4; IR (KBr): 3424, 3280, 2944, 2848, 1558, 1520, 1459, 1401, 1292, 1216, 1068, 956, 777 cm^{-1}; m/z [M+H], 324. Anal. Calcd. for $C_{20}H_{25}N_3O$: C, 74.27; H, 7.79; N, 12.99; Found: C, 74.19; H, 7.76; N, 12.95.

This article is protected by copyright. All rights reserved.

1-(1-cyclohexyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)cyclohexanol (4d)

Yellow solid; mp, 196-197 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.49-2.13 (m, 20H, $10CH_2$) 2.51 (m, 1H, OH), 5.03-5.12 (m, 1H, -CH-N), 5.13 (m, 1H, CH), 6.44 (s, 1H, CH of pyrrole), 7.63-7.68 (m, 2H, 2CH of quinoxaline), 8.11-8.14 (m, 2H, 2CH of quinoxaline); ^{13}C NMR (75 MHz, $CDCl_3$): 21.6, 25.4, 26.6, 30.4, 37.4, 57.8, 71.2, 96.9, 126.2, 126.9, 128.0, 128.6, 128.7, 129.6, 140.0, 157.4; IR (KBr): 3323, 2963, 2834, 1556, 1528, 1483, 1434, 1327, 1112, 755 cm^{-1}; m/z [M+H], 350. Anal. Calcd. for $C_{22}H_{27}N_3O$: C, 74.61; H, 7.79; N, 12.02; Found: C, 74.56; H, 7.81; N, 12.04.

1-(1-(2-hydroxyethyl)-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)cyclohexanol (4e)

yellow solid; mp, 121-123 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28-1.34 (m, 2H, $1CH_2$), 1.56-1.86 (m, 8H, $4CH_2$), 2.02-2.05 (m, 2H, 2OH), 4.13 (t, 2H, J = 4.7, $-NCH_2CH_2OH$), 4.90 (t, 2H, J = 4.7 Hz $-NCH_2CH_2OH$), 6.36 (s, 1H, CH of pyrrole), 7.56-7.62 (m, 2H, 2CH of quinoxaline), 7.93-7.96 (m, 1H, CH of quinoxaline), 8.01-8.04 (m, 1H, CH of quinoxaline); ^{13}C NMR (75 MHz, $CDCl_3$): 21.4, 25.3, 38.0, 46.9, 61.8, 70.9, 97.1, 126.7, 127.6, 127.9, 128.4, 138.4, 140.2, 142.2, 143.5, 159.0; IR (KBr): 3468, 2954, 2934, 1534, 1513, 1445, 1415, 1130, 755 cm^{-1}; m/z [M+H], 312. Anal. Calcd. for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.49; Found: C, 69.51; H, 6.75; N, 13.45.

1-(1-(*p*-tolyl)-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)cyclohexanol (4f)

Yellow solid; mp, 197-200 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.41-1.59 (m, 6H, $3CH_2$), 1.76-1.89 (m, 4H, $2CH_2$), 1.92 (m, 1H, OH), 6.72 (s, 1H, CH pyrrole), 7.29 (s, 4H, ArH), 7.32-7.57 (m, 2H, 2CH of quinoxaline), 7.89-7.93 (m, 1H, CH of quinoxaline), 8.07-8.10 (m, 1H, CH of quinoxaline); ^{13}C NMR (75 MHz, $CDCl_3$): 21.4, 21.6, 25.2, 37.3, 71.9, 98.7, 126.7, 127.3, 128.7, 128.8, 130.0, 130.1, 134.7, 139.1, 139.7, 141.0, 142.1, 145.5, 158.5; IR

This article is protected by copyright. All rights reserved.

Accepted Article

(KBr): 3296, 2944, 2848, 1641, 1513, 1414, 1337, 1132, 1065,755 cm^{-1}; m/z [M+H], 358. Anal. Calcd. for $C_{23}H_{23}N_3O$: C, 77.28; H, 6.49; N, 11.76; Found: C, 77.33; H, 6.50; N, 11.79.

1-(1-phenyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)cyclohexanol (4g)

Yellow solid; mp, 195-198 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.09-1.32 (m, 2H, CH_2), 1.39-1.69 (m, 5H, CH_2), 1.73-1.87 (m, 3H, CH_2), 5.27 (m, 1H, OH), 6.91 (s, 1H, CH pyrrole), 7.51-7.55 (m, 5H, ArH), 7.60-7.72 (m, 2H, 2CH of quinoxaline), 7.89-7.92 (m, 1H, CH of quinoxaline), 8.13-8.16 (m, 1H, Ar-H); ^{13}C NMR (75 MHz, DMSO-d_6): 21.7, 25.5, 36.9, 70.6, 98.4, 127.0, 127.8, 128.5, 129.0, 129.1, 131.1, 138.0, 139.1, 140.8, 142.4, 145.2, 161.2; IR (KBr): 3366, 2956, 2832, 1635, 1582, 1532, 1465, 1414, 1096, 755 cm^{-1}; m/z [M+H], 344. Anal. Calcd. for $C_{22}H_{21}N_3O$: C, 76.94; H, 6.16; N, 12.24; Found: C, 76.90; H, 6.20; N, 12.22.

1-(1-ethyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)-4-methylcyclohexanol (4h)

yellow solid; mp, 180-183 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (d, 3H, CH_3), 1.20-1.34 (m, 2H, CH_2), 1.51 (t, 3H, NCH_2CH_3), 1.60-1.68 (m, 1H, CH), 1.70-1.95 (m, 4H, $2CH_2$), 2.38-2.50 (m, 2H, CH_2), 2.72 (s, 1H, OH), 4.71 (q, 2H, J = 6.8, NCH_2CH_3), 6.60 (s, 1H, CH pyrrole), 7.61-7.70 (m, 2H, 2CH of quinoxaline), 8.12-8.16 (m, 2H, 2CH of quinoxaline); ^{13}C NMR (75 MHz, $CDCl_3$): 15.1, 20.3, 30.4, 30.8, 36.8, 39.5, 71.8, 99.0, 126.3, 127.3, 128.3, 128.7, 139.4, 140.5, 142.3, 143.4, 155.3; IR (KBr): 3398, 2954, 2824, 1530, 1512, 1469, 1415, 1167, 755 cm^{-1}; m/z [M+H], 310. Anal. Calcd. for $C_{19}H_{23}N_3O$: C, 73.76; H, 7.49; N, 13.58; Found: C, 73.66; H, 7.42; N, 13.65.

This article is protected by copyright. All rights reserved.

1-(1-benzyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)-4-methylcyclohexanol (4i)

Yellow solid; mp, 200-203 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.88-2.92 (m, 13H, CH_3, $4CH_2$, CH, OH), 3.57 (s, 2H, NCH_2), 5.93 (s, 1H, CH of pyrrole), 6.93-7.43 (m, 5H, ArH), 7.61-7.72 (m, 2H, 2CH of quinoxaline), 7.99-8.17 (m, 2H, 2CH of quinoxaline); ^{13}C NMR (75 MHz, DMSO-d_6): 20.4, 30.8, 36.7, 47.7, 66.8, 72.0, 100.1, 125.9, 126.5, 126.8, 127.5, 128.5, 128.9, 137.9, 138.8, 139.7, 140.9, 141.9, 148.2, 155.4; IR (KBr): 3421, 2945, 2812, 1643, 1616, 1587, 1545, 1476, 1423, 1045, 755 cm^{-1}; m/z [M+H], 372. Anal. Calcd. for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31; Found: C, 77.62; H, 6.82; N, 11.30.

1-(1-methyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)-2-phenylpropan-1-ol (4j)

Yellow solid; mp, 206-209 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.45 (d, 3H, J = 6.9 Hz, -$CHCH_3$), 3.78 (m, 4H, NCH_3 and OH), 5.08 (m, 1H, $CHCH_3$), 6.03 (d, 1H, J = 5.7 Hz, -CHOH), 6.58 (s, 1H, CH of pyrrole) 7.11-7.31 (m, 5H, ArH), 7.67-7.72 (m, 2H, 2CH of quinoxaline), 8.04-8.09 (m, 2H, 2CH of quinoxaline); ^{13}C NMR (75 MHz, DMSO-d_6): 16.4, 28.6, 45.6, 72.6, 98.3, 126.5, 127.1, 127.5, 127.6, 128.1, 128.5, 128.6, 128.7, 139.0, 140.4, 142.1, 142.4; IR (KBr): 3234, 2935, 2932, 1643, 1587, 1545, 1456, 1413, 1145, 755 cm^{-1}; m/z [M+H], 318. Anal. Calcd. for $C_{20}H_{19}N_3O$: C, 75.69; H, 6.03; N, 13.24; Found: C, 75.60; H, 6.06; N, 13.22.

1-(1-benzyl-1*H*-pyrrolo[2,3-*b*]quinoxalin-2-yl)-2-phenylpropan-1-ol (4k)

Yellow solid; mp, 206-209 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.35 (d, 3H, J = 6.9 Hz, $CHCH_3$), 3.38 (m, 1H, OH), 4.92 (m, 1H, $CHCH_3$), 5.59 (s, 2H, NCH_2), 6.04 (d, 1H, J = 6.3 Hz, CHOH), 6.77 (s, 1H, CH of pyrrole) 7.04-7.35 (m, 5H, ArH), 7.41-7.46 (m, 5H, ArH), 7.67-7.73 (m, 2H, 2CH of quinoxaline), 8.01-8.04 (m, 1H, CH of quinoxaline), 8.10-8.14 (m, 1H, 2CH of quinoxaline); ^{13}C NMR (75 MHz, DMSO-d_6): 16.7, 45.0, 45.1, 71.6, 99.2, 126.4,

This article is protected by copyright. All rights reserved.

Accepted Article

126.6, 126.7, 126.8, 127.6, 128.1, 128.3, 128.4, 128.5, 128.7, 128.8, 137.4, 139.3, 140.7, 141.9, 142.9, 153.9; IR (KBr): 3221, 2965, 2932, 1587, 1545, 1456, 1423, 1135, 755 cm^{-1}; m/z [M+H], 394. Anal. Calcd. for $C_{26}H_{23}N_3O$: C, 79.36; H, 5.89; N, 10.68; Found: C, 79.38; H, 5.88; N, 10.64.

Typical experimental procedure for synthesis of 1-((3-((cyclo)alkylamino)quinoxalin-2-yl)ethynyl)cyclohexanol (5a-b)

The mixture of a cyclohexanone (1 mmol), Cs_2CO_3 (0.5 mmol) and calcium carbide (2.5 mmol) DMSO-H_2O (5:0.1 mL) was stirred at 60 ºC for 8 hours. After completion of the reaction (8 h) an *N*-alkyl-3-chloroquinoxaline-2-amine (0.5 mmol), $Pd(PPh_3)_2Cl_2$ (0.05 mmol), and Triethylamine (3.0 mmol) were added, respectively. Stirring the reaction mixture was continued for another 2-3 h at 60 ºC. After completion of the reaction (monitored by TLC), the solvent was evaporated, and the remaining solid was washed with H_2O and then dried. The crude product was purified by column chromatography (silica gel 100) using *n*-hexane/ethyl acetate (80/20).

1-((3-(butylamino)quinoxalin-2-yl)ethynyl)cyclohexanol (5a)

Yellow solid; mp, 103-106 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.95 (t, J = 7.5 Hz, 3H, $NHCH_2CH_2CH_2CH_3$), 1.32-1.57 (m, 6H, $3CH_2$), 1.60-1.74 (m, 6H, CH_2), 1.94-1.97 (m, 2H, $NHCH_2CH_2CH_2CH_3$), 3.50-3.55 (m, 2H, $NHCH_2CH_2CH_2CH_3$), 5.83 (m, 1H, OH), 6.58 (t, J = 6.0, 1H, $NHCH_2CH_2CH_2CH_3$), 7.35-7.40 (m, 1H, CH of quinoxaline), 7.58-7.61 (m, 2H, 2CH of quinoxaline), 7.75-7.77 (m, 1H, CH of quinoxaline); ^{13}C NMR (75 MHz, DMSO-d_6): 14.2, 20.2, 23.1, 25.2, 31.2, 39.5, 40.6, 67.5 78.5, 102.5, 124.6, 126.1, 128.6, 130.8, 130.9, 136.3, 141.2, 151.7; IR (KBr): 3424, 2928, 2848, 1696, 1600, 1516, 1408, 1318, 1110, 752

This article is protected by copyright. All rights reserved.

cm^{-1}; m/z [M+H], 324. Anal. Calcd. for $C_{20}H_{25}N_3O$: C, 74.27; H, 7.79; N, 12.99; Found: C, 74.32; H, 7.81; N, 12.92.

1-((3-(cyclohexylamino)quinoxalin-2-yl)ethynyl)cyclohexanol (5b)

Yellow solid; mp, 110-113 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28-2.18 (m, 21H, 10CH_2 and OH), 4.11-4.17 (m, 1H, CH), 7.24-7.30 (m, 1H, CH of quinoxaline), 7.42-7.48 (m, 2H, 2CH of quinoxaline), 7.56-7.60 (m, 1H, CH of quinoxaline); ^{13}C NMR (75 MHz, $CDCl_3$): 20.5, 23.9, 24.8, 30.6, 30.9, 31.5, 49.2, 66.2, 85.6, 103.5, 123.6, 124.7, 127.6, 138.3, 138.6, 139.0, 139.4, 148.2; IR (KBr): 3423, 2963, 2834, 1656, 1568, 1523, 1483, 1414, 1112, 755 cm^{-1}; m/z [M+H], 350. Anal. Calcd. for $C_{22}H_{27}N_3O$: C, 75.61; H, 7.79; N, 12.02; Found: C, 75.66; H, 7.82; N, 11.98.

Characterization data for 6 and 7

3,3'-(ethyne-1,2-diyl)bis(*N*-ethylquinoxalin-2-amine) (6h)

Yellow solid; mp, 100-103 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.24 (t, J = 6.9 Hz, 3H, $NHCH_2CH_3$), 3.51-3.55 (m, 2H, $NHCH_2CH_3$), 7.39-7.40 (m, 2H, CH of quinoxaline and $NHCH_2CH_3$), 7.62-7.63 (m, 2H, 2CH of quinoxaline), 7.79-7.81 (m, 1H, CH of quinoxaline); IR (KBr): 3388, 2954, 2821, 1520, 1512, 1469, 1418, 1167, 755 cm^{-1}; m/z [M+H], 369. Anal. Calcd. for $C_{22}H_{20}N_6$: C, 71.72; H, 5.47; N, 22.81; Found: C, 71.75; H, 5.40; N, 22.79.

3-(propylamino)quinoxalin-2(1*H*)-one (7b)

Yellow solid; mp, 140-142 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07 (t, J = 7.4 Hz, 3H, $NHCH_2CH_2CH_3$), 1.71-1.82 (m, 2H, $NHCH_2CH_2CH_3$), 3.55 (t, J = 6.7 Hz, 2H, $NHCH_2CH_2CH_3$), 6.34 (s, 1H, $NHCH_2CH_2CH_3$), 7.16-7.28 (m, 3H, CH of quinoxaline),

This article is protected by copyright. All rights reserved.

Accepted Article

7.54-7.57 (m, 1H, CH of quinoxaline), 11.16 (s, 1H, NH-CO); IR (KBr): 3408, 2976, 2928, 1667, 1574, 1526, 1497, 1465, 1382, 1241, 1206, 748 cm^{-1}; m/z [M+H], 204. Anal. Calcd. for $C_{12}H_{15}N_3$: C, 71.61; H, 7.51; N, 20.88; Found: C, 71.58; H, 7.54; N, 20.86.

Acknowledgment

We gratefully acknowledge the financial support of the Research Council of the Shahrood University of Technology.

Supporting information

Supporting information for this work is available: copies of ^{1}H and ^{13}C spectra of all the new compounds.

References

[1] (a) I.-T. Trotus¸, T. Zimmermann, F. Schu¨th, *Chem. Rev.* **2013**, *114*, 1761; (b) W. Wu, H. Jiang, *Acc. Chem. Res.* **2014**, *47*, 2483; (c) R. Jira, *Angew. Chem., Int. Ed.* **2009**, *48*, 9034; (d) R. Chinchilla, C. Najera, *Chem. Rev.* **2013**, *114*, 1783.

[2] K. S. Rodygin, G. Werner, F. A. Kucherov, V. P. Ananikov, *Chem. Asian J.* **2016**, *11*, 965.

[3] W. Zhang, H. Wu, Z. Liu, P. Zhong, L. Zhang, X. Huang, J. Cheng, *ChemComm.* **2006**, 4826.

[4] D. Yu, Y. N. Sum, A. C. C. Ean, M. P. Chin, Y. Zhang, *Angew. Chem., Int. Ed.* **2013**, *52*, 5125.

[5] Y. N. Sum, D. Yu, Y. Zhang, *Green Chem.* **2013**, *15*, 2718.

[6] Z. Lin, D. Yu, Y. N. Sum, Y. Zhang, *ChemSusChem* **2012**, *5*, 625.

[7] (a) P. Chuentragool, K. Vongnam, P. Rashatasakhon, M. Sukwattanasinitt, S.

This article is protected by copyright. All rights reserved.

Accepted Article

Wacharasindhu, *Tetrahedron* **2011**, *67*, 8177; (b) W. Zhang, H. Wu, Z. Liu, P. Zhong, L. Zhang, X. Huang, J. Cheng, *ChemComm.* **2006**, 4826.

[8] (a) Q. Yang, Y. Jiang, C. Kuang, *Helv. Chim. Acta* **2012**, *95*, 448; (b) Y. Jiang, C. Kuang, Q. Yang, *Synlett* **2009**, *2009*, 3163.

[9] D. Yu, Y. N. Sum, A. C. C. Ean, M. P. Chin, Y. Zhang, *Angew. Chem., Int. Ed.* **2013**, *52*, 5125.

[10] A. C. Götzinger, F. A. Theßeling, C. Hoppe, T. J. Müller, *J. Org. Chem.* **2016**, *81*, 10328.

[11] A. C. Götzinger, T. J. Müller, *Org. Biomol. Chem.* **2016**, *14*, 3498.

[12] K. Sonogashira, *J. Org. Chem.* **2002**, *653*, 46.

[13] (a) I. Paterson, R. D. Davies, R. Marquez, *Angew. Chem.* **2001**, *113*, 623; (b) M. Toyota, C. Komori, M. Ihara, *J. Org. Chem.* **2000**, *65*, 7110; (c) F. Yoshimura, S. Kawata, M. Hirama, *Tetrahedron Lett.* **1999**, *40*, 8281.

[14] (a) K. Nicolaou, A. C. Dai WM, *Chem. Rev.* **2005**, *105*, 739; (b) J. W. Grissom, G. U. Gunawardena, D. Klingberg, D. Huang, *Tetrahedron* **1996**, *52*, 6453.

[15] (a) R. Wu, J. S. Schumm, D. L. Pearson, J. M. Tour, *J. Org. Chem.* **1996**, *61*, 6906; (b) U. H. Bunz, *Chem. Rev.* **2000**, *100*, 1605.

[16] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467.

[17] (a) M. Kotora, T. Takahashi, *Palladium-Catalyzed Homocoupling of Organic Electrophiles or Organometals*; Wiley Online Library, **2002**; (b) P. Siemsen, R. C. Livingston, F. Diederich, *Angew. Chem., Int. Ed.* **2000**, *39*, 2632.

[18] J. Cheng, Y. Sun, F. Wang, M. Guo, J.-H. Xu, Y. Pan, Z. Zhang, *J. Org. Chem.* **2004**, *69*, 5428.

[19] A. Elangovan, Y.-H. Wang, T.-I. Ho, *Org. Lett.* **2003**, *5*, 1841.

[20] S. Thorand, N. Krause, *J. Org. Chem.* **1998**, *63*, 8551.

This article is protected by copyright. All rights reserved.

Accepted Article

Accepted Article

[21] D.-H. Lee, H. Qiu, M.-H. Cho, I.-M. Lee, M.-J. Jin, *Synlett* **2008**, *2008*, 1657.

[22] D. H. Lee, Y. J. Kwon, M. J. Jin, *Adv. Synth. Catal.* **2011**, *353*, 3090.

[23] C. Torborg, J. Huang, T. Schulz, B. Schaeffner, A. Zapf, A. Spannenberg, A. Boerner, M. Beller, *Chemistry-A European Journal* **2009**, *15*, 1329.

[24] Y. Yang, X. Chew, C. W. Johannes, E. G. Robins, H. Jong, Y. H. Lim, *Eur. J. Org. Chem.* **2014**, *2014*, 7184.

[25] H. Zhong, J. Wang, L. Li, R. Wang, *Dalton Trans.* **2014**, *43*, 2098.

[26] N. E. Leadbeater, B. J. Tominack, *Tetrahedron Lett.* **2003**, *44*, 8653.

[27] V. P. Böhm, W. A. Herrmann, *Eur. J. Org. Chem.* **2000**, *2000*, 3679.

[28] K. W. Anderson, S. L. Buchwald, *Angew. Chem., Int. Ed.* **2005**, *44*, 6173.

[29] C. Yi, R. Hua, *J. Org. Chem.* **2006**, *71*, 2535.

[30] Y. Luo, H. Gao, Y. Li, W. Huang, W. Lu, Z. Zhang, *Tetrahedron* **2006**, *62*, 2465.

[31] C. A. Fleckenstein, H. Plenio, *Green Chem.* **2008**, *10*, 563.

[32] A. Chandra, B. Singh, S. Upadhyay, R. M. Singh, *Tetrahedron* **2008**, *64*, 11680.

[33] X. Pu, H. Li, T. J. Colacot, *J. Org. Chem.* **2013**, *78*, 568.

[34] D. M. D'Souza, T. J. Mueller, *Chem. Soc. Rev.* **2007**, *36*, 1095-1108.

[35] C. M. Volla, I. Atodiresei, M. Rueping, *Chem. Rev.* **2013**, *114*, 2390-2431.

[36] J. S. Quesnel, B. A. Arndtsen, *Pure Appl. Chem.* **2013**, *85*, 377-384.

[37] A. Huang, C. Ma, *Mini-Rev. Med. Chem.* **2013**, *13*, 607.

[38] A. Keivanloo, M. Bakherad, A. Rahimi, S. A. N. Taheri, *Tetrahedron Lett.* **2010**, *51*, 2409.

[39] A. Keivanloo, M. Bakherad, A. Rahimi, *Synthesis* **2010**, *2010*, 1599.

[40] A. Keivanloo, M. Bakherad, M. Rahmani, A. Rahimi, *Monatsh. Chem.* **2013**, *144*, 859.

[41] (a) A. Keivanloo, S. S. Kazemi, H. Nasr-Isfahani, A. Bamoniri. *Tetrahedron* **2016**,

This article is protected by copyright. All rights reserved.

72, 6536; (b) S. S. Kazemi, A. Keivanloo, H. Nasr-Isfahani, A. Bamoniri, *RSC Adv.* **2016**, *6*, 92663; (c) T. Besharati-Seidani, A. Keivanloo, B. Kaboudin, T. Yokomatsu, *RSC Adv.* **2016**, *6*, 83901; (d) A. Keivanloo, S. S. Kazemi, H. Nasr-Isfahani, A. Bamoniri, Mol. Divers. **2017**, *21*, 29.

[42] A. Soozani, A. Keivanloo, M. Bakherad, *ChemistrySelect* **2017**, *2*, 9701.

[43] A. Hosseini, D. Seidel, A. Miska, P. R. Schreiner, *Org. Lett.* **2015**, *17*, 2808.

Accepted Article

This article is protected by copyright. All rights reserved.