Organic & Biomolecular Chemistry

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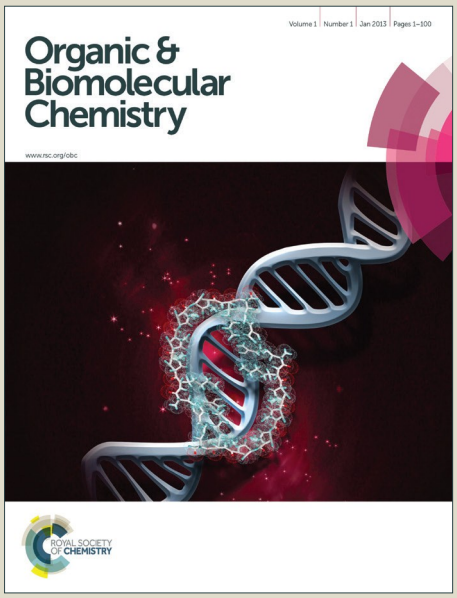

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DOI: 10.1039/C6OB00226A

Journal Name

ARTICLE

Copper-catalyzed radical reactions of 2-azido-*N*-arylacrylamides with 1-(trifluoromethyl)-1,2-benziodoxole and 1-azidyl-1,2-benziodoxole

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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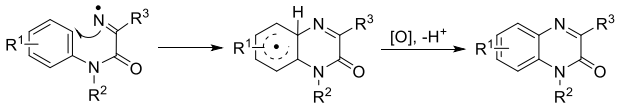
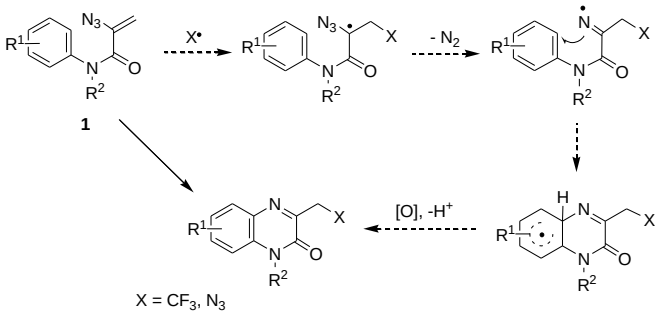
The reactions of 2-azido-*N*-arylacrylamides with the trifluoromethyl radical and azidyl radical were investigated by using Togni's reagent and Zhdankin's reagent as the source of these radicals. Under the catalysis of CuI, Togni's reagent was firstly converted to the trifluoromethyl radical, which then reacted with 2-azido-*N*-arylacrylamides to afford the corresponding α-(arylaminocarbonyl)iminyl radicals. The cyclization of the iminyl radicals delivered quinoxalin-2(1*H*)-one products in moderate yields. Similar reaction took place between 2-azido-*N*-arylacrylamides and the azidyl radical. In the latter cases, the reaction produced 3-azidomethyl and 3-cyano-subsituted quinoxalin-2(1*H*)-ones. This study not only helps elucidate the factors influencing the cyclization of α-(arylaminocarbonyl)iminyl radicals, but also provides a new approach towards quinoxalin-2-ones.

Introduction

Iminyl radicals are valuable intermediates in the synthesis of nitrogen heterocycles.[1] Recent studies by Spagnolo et al.,[2] Zhang et al.[3] and our own[4] demonstrate that the cyclisation of the α-(arylaminocarbonyl)iminyl radical would deliver the quinoxalin-2(1*H*)-one ring structure (Scheme 1). As quinoxalin-2-one is an important heterocyclic skeleton that appears in many biologically and pharmaceutically significant compounds,[5] this reaction holds promise to become a highly useful synthetic tool. Despite these encouraging results, however, previous investigations indicate that the efficacy of this approach is largely influenced by the reaction conditions and the structural features of the iminyl radical. Considering the substituent effect adjacent to the iminyl radical center (R^3), the yields are generally high when R^3 is an ethoxycarbonyl group,[4] but are much lower when it becomes an alkyl group.[2] On the other hand, when an aryl group is attached to the iminyl radical, no quinoxalin-2-one product could be generated.[4,6] In an attempt to further expand the scope of this reaction, we investigated the tandem radical addition/cyclization reaction of vinyl azides with trifluoromethyl radical[7] and azidyl radical[8] (Scheme 2). Recent studies by Chiba et al.[9] Spagnolo, et al.,[10] and Zhou, et al.[11] show that iminyl radicals can be conveniently prepared from addition of a radical to vinyl azides followed by extrusion of a nitrogen molecule. We envisioned that by using this strategy, the cyclization of alkyl substituted α-(arylaminocarbonyl)iminyl radicals could be further evaluated with regard to the substituent effect. Moreover, as both trifluoromethyl[12] and azidyl[13] groups are important functional groups, a new method for the preparation of trifluoromethyl and azidyl-functionalized quinoxalin-2(*1H*)-ones will be synthetically useful. By using 1-(trifluoromethyl)-1,2-benziodoxole (Togni's reagent) as the source of trifluoromethyl radical and 1-azidyl-1,2-benziodoxole (Zhdankin's reagent) as the source of azidyl radical, we implemented this idea, and herein we wish to report our result.



Scheme 1 An approach towards quinoxalin-2(*1H*)-one moiety via the cyclization of α-(arylaminocarbonyl)iminyl radicals



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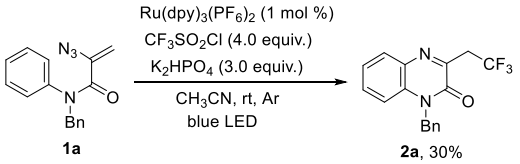
Electronic Supplementary Information (ESI) available: [General methods, experimental procedures, characterization data, ^{1}H NMR and ^{13}C NMR spectra]. See DOI: 10.1039/x0xx00000x

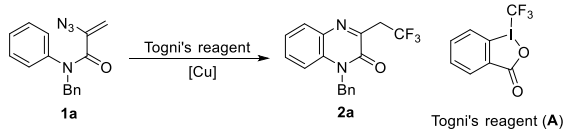
Scheme 2 Design of this work

Results and discussion



Scheme 3 Reaction of **1a** with CF_3SO_2Cl under visible light irradiation

Table 1 Screening of the reaction conditions with Togni' reagent [a]



Entry	Cat.	Equiv. of **A**	Sovlent	Temp. (°C)	Yield of **2a**[b]
1	CuI	2.0	CH_3OH	80	30
2	CuCl	2.0	CH_3OH	80	44
3	CuTc	2.0	CH_3OH	80	24
4	CuTc	2.0	CH_3OH	80	48
5	$CuCl_2$	2.0	CH_3OH	80	N.R.[c]
6	$Cu(OAc)_2$	2.0	CH_3OH	80	32
7	Cu powder	2.0	CH_3OH	80	32
8	CuI	2.0	toluene	80	58
9	CuCl	2.0	toluene	80	36
10	CuBr	2.0	toluene	80	30
11	CuBr·SMe_2	2.0	toluene	80	--[d]
12	CuTc	2.0	toluene	80	25
13	$CuCl_2$	2.0	toluene	80	N.R.[c]
14	$Cu(OAc)_2$	2.0	toluene	80	23[e]
15	Cu powder	2.0	toluene	80	46[e]
16	CuI	2.0	toluene	60	57[e]
17	CuI	2.0	toluene	100	26[d]
18	CuI	3.0	toluene	80	60[e]
19	***CuI***	***4.0***	***toluene***	***80***	***67***[e]
20	CuI	2.0	DCE	80	48[e]
21	CuI	2.0	CH_3CN	80	mixture[f]
22	CuI	2.0	DMF	80	mixture[f]
23	CuI	2.0	$CHCl_3$	80	N.R.[c]

[a] The reaction was carried out on a 0.2 mmol scale in 2 mL solvent under an argon atmosphere. 10 mol % of copper catalyst was used unless otherwise specified. [b] NMR yield with 1,4-dioxane as an internal standard unless otherwise specified. [c] No reaction took place. [d] **1a** decomposed. [e] Isolated yield. [f] Complex mixture was obtained. CuTc: copper(I) thiophene-2-carboxylate. DCE: 1,2-dichloroethane.

We began our study by examining the reaction of 2-azido-*N*-benzyl-*N*-phenylacrylamide (**1a**) with the trifluoromethyl radical. Firstly, CF_3SO_2Cl was used as the source of trifluoromethyl radical, and was allowed to react with **1a** under the recently developed visible light irradiation conditions.[14] As expected, the desired reaction took place, but the yield of quinoxalin-2-one product **2a** was low (Scheme 3). After some futile attempts to improve yield, we next chose Togni's reagent as the trifluoromethylating agent.[15] Recent studies demonstrate that Togni's reagent constitutes a reliable source of the trifluoromethyl radical, and is applicable to a variety of transformations.[16] Copper salts are suitable catalysts to engender the generation of the trifluoromethyl radical from Togni's reagent. Thus, on the basis of recent studies, we tested some commonly used copper salts for their catalytic capacity on the reaction of **1a** with Togni's reagent (**A**), and the results are summarized in Table 1.

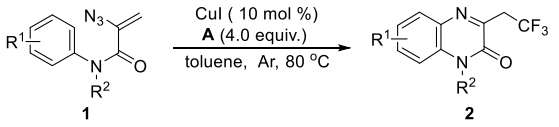
As can be seen in Table 1, among the copper catalysts examined, all can catalyze the desired reaction to afford **2a** except $CuCl_2$ and CuBr·SMe_2, but using CuI delivered the best result when the reaction proceeded in toluene at 80 °C (Table 1, entry 8). The yield of **2a** reached 67% by using 4.0 equiv. of **A** (Table 1, entry 19). Lowering the reaction temperature would extend the reaction time (Table 1, entry 16), whereas raising the temperature to 100 °C resulted in the decrease in the yield of **2a** (Table 1, entry 17).

The optimized reaction conditions (Table 1, entry 19) were then applied to variously substituted 2-azido-*N*-arylacrylamides (**1**), and the results are listed in Table 2. All the *para* and *meta*-substituted compounds except compound **1g** were transformed to trifluoromethyl-attached quinoxalin-2-ones **2**, while the desired reaction failed to occur to *ortho*-substituted compounds **1n**-**1q** (Table 2, entries 14-17). In the latter cases, most of the substrate was recovered after 18 h, indicating that the presence of an *ortho*-substituent would prohibit **1** from reacting with trifluoromethyl radical. For the reaction of **1a**, the yield was a little lower on 0.5 mmol scale than that shown in Table 1 (on 0.2 mmol scale). It is interesting to see that when *meta*-substituted **1h**-**1m** was used as the substrates, different selectivities were observed: in the cases of **1i**, **1j**, **1l** and **1m**, 5-substituted isomers **2-1** were obtained as the only isolable product, whereas the reaction of iodine-substituted **1k** afforded only 7-substituted isomer **2k-2**. On the other hand, both isomers were obtained when **1h** was used as the substrate. Our previous studies indicates that cyclization of the α-(arylaminocarbonyl)iminyl radical is of *ortho*-selectivity, that is, the attack prefers to take place at the sterically more crowded dual *ortho* position. The result with **1i**, **1j**, **1l** and **1m** is consistent with our previous observation.[4] The abnormal selectivity in the case of **1k** (Table 2, entry 11) remains unclear at this stage.

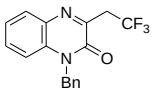
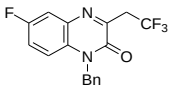
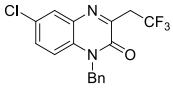
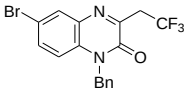
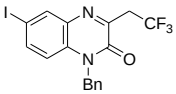
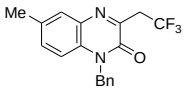
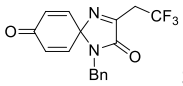
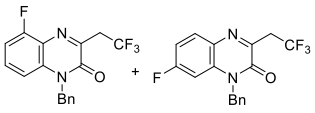
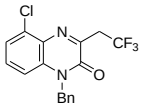
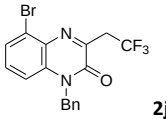
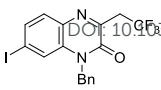
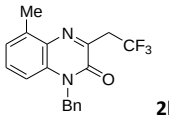
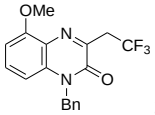
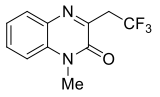
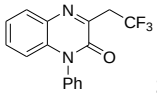
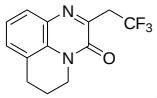
Unlike other substrates, compound **1g** reacted to give spirocyclohexadienones **3g** rather than the corresponding quinoxalin-2-one product (Table 2, entry 7). The formation of compound **3g** involved an azaspirocyclohexadienyl carbocation intermediate, with an azaspirocyclohexadienyl radical being its precursor. Similar result was also obtained in our previous study.[4]

Besides the above-mentioned results, it can also be seen in Table 2 that replacement of benzyl with aryl or other alkyl *N*-substituent would cause no substantial change in quinoxalin-2-one production (Table 2, entries 18-20).

Table 2 CuI-catalyzed reaction of **1** with Togni's reagent [a]



1 **2**

Entry	Sub.	R^1	R^2	Product(s) (Yield, %)[b]
1	**1a**	H	Bn	 **2a** (64)
2	**1b**	*p*-F	Bn	 **2b** (50)
3	**1c**	*p*-Cl	Bn	 **2c** (56)
4	**1d**	*p*-Br	Bn	 **2d** (48)
5	**1e**	*p*-I	Bn	 **2e** (38)[c]
6	**1f**	*p*-Me	Bn	 **2f** (41)
7	**1g**	*p*-OMe	Bn	 **3g** (60)
8	**1h**	*m*-F	Bn	 **2h-1** (29), **2h-2** (38)
9	**1i**	*m*-Cl	Bn	 **2i-1** (38)
10	**1j**	*m*-Br	Bn	 **2j-1** (53)
11	**1k**	*m*-I	Bn	 **2k-2** (34)
12	**1l**	*m*-Me	Bn	 **2l-1** (57)
13	**1m**	*m*-OMe	Bn	 **2m-1** (60)
14	**1n**	*o*-F	Bn	N.R.[d]
15	**1o**	*o*-Cl	Bn	N.R.[d]
16	**1p**	*o*-Me	Bn	N.R.[d]
17	**1q**	*o*-OMe	Bn	N.R.[d]
18	**1r**	H	Me	 **2r** (60)
19	**1s**	H	Ph	 **2s** (48)
20	**1t**	*o*-$(CH_2)_3$-(N)		 **2t** (56)

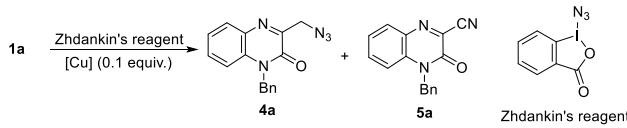
[a] Reaction conditions: A mixture of 0.5 mmol of **1**, 1.0 mmol of **A** and 0.05 mmol of CuI in 5 mL of anhydrous toluene was stirred at 80 °C under an argon atmosphere for 18 h. [b] Isolated yield. [c] **2e** was accompanied by a minor amount of 1-benzyl-6-iodo-3-(iodomethyl)quinoxalin-2(1*H*)-one (yield: 9%). Similar 3-(iodomethyl)quinoxalin-2(1*H*)-one by products were also detected in tiny amount in the reactions of other substrates. [d] No reaction took place. Most of the substrate was recovered.

Following our investigation on the reaction of **1** with trifluoromethyl radical, we went on to see if azidyl radical could react with **1** in the same way.[17] We employed Zhdankin's reagent as the source of azidyl radical. As an analogue of Togni's reagent, Zhdankin's reagent also has the merit of good thermal stability and high reactivity, and thus has found wide applications in the azidation of manifold organic compounds.[18] Like Togni's reagent, Zhdankin's reagent can also be reduced by Cu(I) to give the azidyl radical.[18d,18e] In our subsequent study, we first tested some conditions for the copper-catalyzed reaction of **1a** with Zhdankin's reagent (**B**), and the results are summarized in Table 3.

As shown in Table 3, toluene was found to be the suitable solvent, and the optimal reaction temperature was 40–60 °C. Two products, **4a** and **5a**, were obtained, and their ratio was largely influenced by the catalyst used. When CuI was used as the catalyst, both **4a** and **5a** were obtained, with the latter being the major product. However, the CuTc-catalyzed

reaction afforded only **4a**, even after long reaction time (Table 3， entry 17). By contrast, when the catalyst became Cu powder or $Cu(OAc)_2$, only compound **5a** was obtained after 24 h (Table 3，entries 18 and 19). Control experiment indicates that compound **5a** derived from **4a** by oxidation and denitrogenation.[19]

Table 3 Screening of the conditions for the reaction of 1a with Zhdankin's reagent [a]



Entry	[Cu]	Solvent	Temp. (°C)	Time (h)	Yield of **4a** and **5a** (%)[b]
1	CuI	toluene	40	6	18 (**4a**)[c], 40 (**5a**)[c]
2	CuI	methanol	40	8	13 (**4a**), 31 (**5a**),
3	CuI	toluene	40	6	23 (**4a**), 44 (**5a**)
4	CuI	toluene	rt	24	17 (**4a**)[c], 41 (**5a**)[c]
5	CuI	methanol	rt	16	15 (**4a**)[c], 29 (**5a**)[c]
6	***CuI***	***toluene***	***60***	***4***	***15 (4a)[c], 44 (5a)[c]***
7	CuI	toluene	80	4	--[d]
8[e]	CuI	toluene	40	6	<1 (**4a**)[c], 39 (**5a**)[c]
9	CuI	DCE	40	6	23 (**4a**), <1 (**5a**)
10	CuI	DMSO	40	6	19 (**4a**), <1 (**5a**)
11	CuI	DMF	40	2	mixture[f]
12	CuI	CH_3CN	40	6	mixture[f]
13	CuI	$CHCl_3$	40	6	N. R.[g]
14	CuI	THF	40	6	N. R.[g]
15	$Cu(CN)_4PF_6$	methanol	40	24	mixture[f]
16	$Cu(CN)_4PF_6$	toluene	40	24	N. R.[g]
17	CuTc	toluene	40	24	43 (**4a**), <1 (**5a**)
18	Cu powder	toluene	40	24	< 1 (**4a**), 29 (**5a**)
19	$Cu(OAc)_2$	toluene	40	24	<1(**4a**), 38 (**5a**)

[a] The reaction was carried out on a 0.2 mmol scale in 2 mL solvent. 2.0 Equiv. of **B** was used unless otherwise specified, [b] NMR yield with 1,4-dioxane as an internal standard. [c] Isolated yield. [d] **1a** Decomposed. [e] 3.0 Equiv. of **B** was used. [f] Complex mixture was obtained. [g] No Reaction took place.

The CuI-mediated reaction conditions (Table 3, entry 6) were then applied to other substrates **1**, and the results were illustrated in Table 4. Like the reactions with Togni's reagent, most of the *para* and *meta* substituted substrates reacted to deliver quinoxalin-2-one products, but the *ortho*-substituted compounds failed to react under the same conditions. Among the *para*-substituted substrates (Table 4, entries 2-7), **1b**, **1c** and **1f** reacted to afford a mixture of **4** and **5**, while **1d** and **1e** were converted thoroughly to the 3-cyano-substituted **5d** and **5e** at the time when the substrate was completely consumed. The low yield for the reaction of **1f** can be attributed to the decomposition of the products, as compound **5f** was found to be very unstable.[20] On the other hand, no isolable product was obtained in the case of **1g**. For the *meta*-substituted **1h**-**1m**, the composition of the products was complicated because of the formation of the regio-isomers. Moreover, it was also largely influenced by the electronic nature of the substituent. When **1l** or **1m** was used as the substrate, three products were obtained for each reaction. Unfortunately, these products, except **4l-1** and **5m-1**, are very unstable; their decomposition was observed (by color change) during the preparation of sample for NMR measurement.[20] Overall, these results of indicate that the transformation from **4** to **5** is sensitive to the substituent effect at the benzene ring, which also has a big influence on the stability of **4** and **5**. Despite the instability of some of these products, however, the regioselectivities of the reactions of **1h**-**1l** shown in Table 4 are in general consistent with those exhibited in the trifluoromethylation reactions (Table 2). Besides the substituent effect illustrated above, the current reaction is susceptible to other structural change. As such, the reaction of **1r** gave only compound **5r** as the only isolable product (which is also unstable), whereas **1t** decomposed completely under the same conditions.

The CuI-catalyzed reactions of compounds **1** with Togni's reagent and Zhdankin's reagent can be rationalized with a mechanism shown in Scheme 4. The yields of the quinoxalin-2-one products were in general moderate, but significantly higher than those reported by Spagnolo et al.[2] for cyclization of other 1-alkyl-(arylaminocarbonyl)iminyl radicals under reductive conditons. The instability of the products is partly responsible for the low yield exhibited in Table 4, but in general the current reactions reflect a demonstrable structural influence on the cyclization step. Both the trifluoromethyl and azidyl are electron withdrawing groups, and they can affect the cyclization by enhancing the electrophilicity of the iminyl radical. However, this effect is much weaker than that of ethoxycarbonyl group in radical **R-e**.[4] The present results, in combination with these previous studies, corroborate that an adjacent electron withdrawing group is beneficial to the cyclization of α-(arylaminocarbonyl)iminyl radicals. Furthermore, in the current cases steric hindrance by trifluorethyl and azidomethyl substituent possibly caused some negative influence on the cyclization of corresponding iminyl radicals. In fact, previous studies suggest that quinoxalin-2-one-forming cyclization of α-(arylaminocarbonyl)iminyl radicals could be (notably) depressed in the presence of an adjacent alkyl or aryl group.[2-4] The addition of trifluoromethyl or azidyl radicals on the carbon-carbon double bond in **1**, on the other hand, should be an efficient process, as these radicals can add facilely to various functionalized olefins, including *N*-arylacrylamides.[17b-d, 21]

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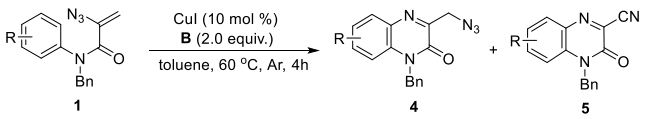
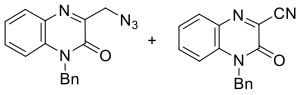
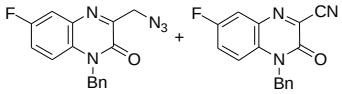
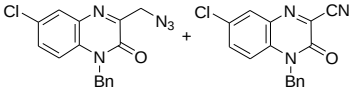
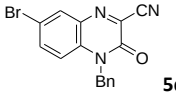
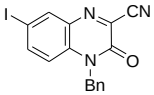
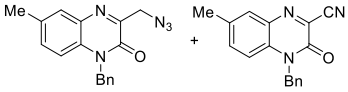
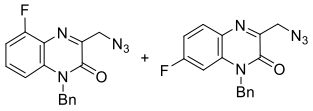
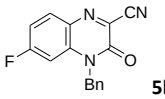
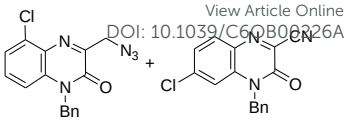
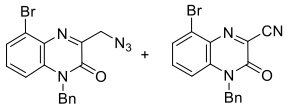
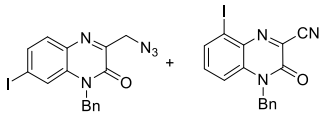
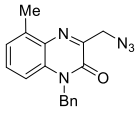
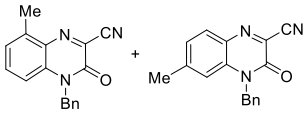
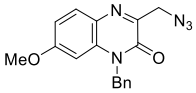
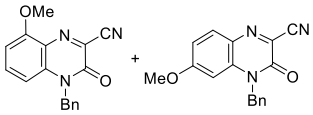
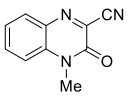
DOI: 10.1039/C6OB00226A

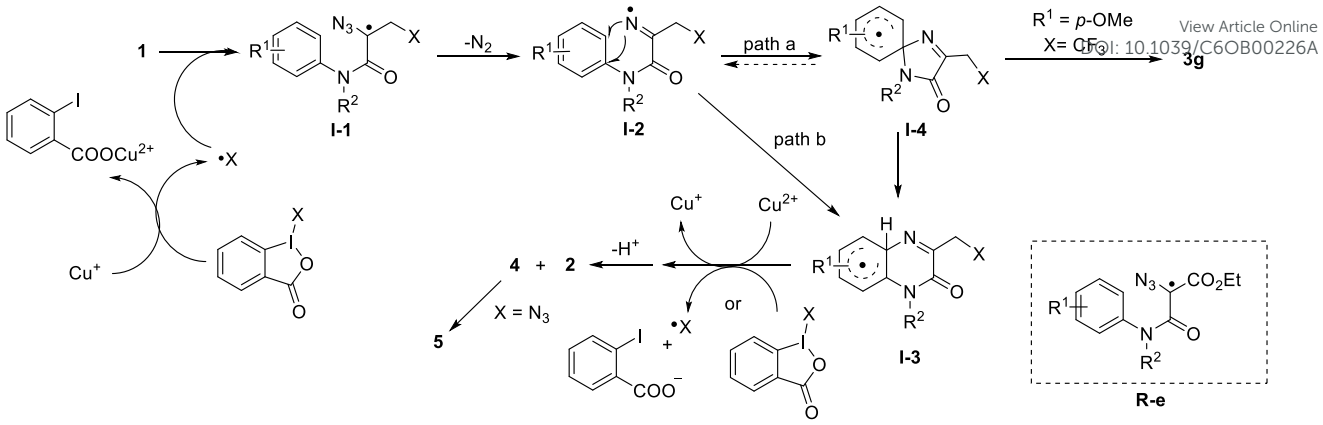
Table 4 CuI-catalyzed reaction of 1 with Zhdankin's reagent [a]



1 4 5

Entry	Sub.	Time (h)[c]	Products (Yield, %)[b]
1	**1a**	6	 **4a** (12), **5a** (44)
2	**1b**	6	 **4b** (15), **5b** (19)
3	**1c**	10	 **4c** (15), **5c** (44)
4	**1d**	12	 **5d** (42)
5	**1e**	18	 **5e** (48)
6	**1f**	4	 **4f** (9) , **5f** (22)[c]
7	**1g**	4	--[d]
8	**1h**	6	 **4h-1** + **4h-2** (2:5,[e] 17)  **5h-2** (16)
9	**1i**	10	 **4i-1** + **5i-2** (3:2,[d] 46)
10	**1j**	12	 **4j-1** + **5j-1** (3:1,[e] 34)
11	**1k**	18	 **4k-2** + **5k-1** (5:1,[e] 47)
12	**1l**	4	 **4l-1** (40)  **5l-1** + **5l-2** (10:9,[e] 32)[c]
12	**1m**	3.5	 **4m-2** (15)[c]  **5m-1** (34), **5m-2** (12)[c]
13	**1n**	12	N.R.[f]
14	**1o**	12	N.R.[f]
15	**1r**	6	 **5r** (30)[c]
16	**1t**	6	--[d]

[a] Reaction conditions: A mixture of 0.5 mmol of **1**, 1.0 mmol of **B** and 0.05 mmol of CuI in 5 mL of anhydrous toluene was stirred at 80 °C under an argon atmosphere. The reaction was quenched when **1** was consumed completely (indicated by TLC). [b] Isolated yield. [c] This compound is unstable.[20] [d] **1** decomposed. [e] The ratio of the products was determined by ^{1}HNMR. [f] No reaction took place. Most of the substrate was recovered.



Scheme 4 Plausible mechanism for the reactions of **1** with Tongi's reagent and Zhdankin's reagent.

Conclusions

In summary, we have demonstrated that 2-azido-*N*-arylacrylamides can react with trifluoromethyl radical *via* a tandem addition/cyclization process to afford trifluoromethyl-functionalized quinoxalin-2-ones. Togni's reagent was used herein as the source of trifluoromethyl radical. Similar reaction took place between 2-azido-*N*-arylacrylamides and Zhdankin's reagent. In the latter cases, the reaction would produce 3-azidomethyl and/or 3-cyano-subsituted quinoxalin-2(*1H*)-ones. Both reactions involve α-(arylaminocarbonyl) iminyl radicals as key intermediates, from which quinoxalin-2-one products are formed via cyclization. The yields of these reactions are in general moderate, which can be ascribed to influences of both the electronic effect and steric effect around the iminyl radical center. Besides the mechanistic implications, the current study provides a new approach to gain access to functionalized quinoxalin-2-ones.

Experimental

General procedure for the preparation of 2-azido-*N*-arylacrylamides (1)

2-Azido-*N*-arylacrylamides were prepared from arylamines in two steps following the procedure given below.

To a stirred solution of the arylamine (15 mmol) in 30 mL CCl_4 was added a solution of 2,3-dibromopropanoyl chloride (15 mmol, 3.75 g) in 10 mL CCl_4 over 30 min at ice-salt baths. The mixture was stirred at room temperature for 12 h. After that, the mixture was poured into a saturated aqueous $NaHCO_3$ solution (50 mL), and the aqueous phase was extracted with CH_2Cl_2 (3× 30 mL). The combined organic phases were then washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure on a rotary evaporator. The thus obtained crude product was purified by column chromatography on silica gel (with petroleum ether and ethyl acetate (15:1) as effluent unless otherwise specified) to give 2,3-dibromo-*N*-aryllpropanamide.[22]

A solution of thus prepared 2,3-dibromo-*N*-aryllpropanamide (10 mmol) and NaN_3 (12 mmol, 0.78 g) in DMSO (50 mL) was stirred overnight at room temperature under an argon atmosphere. Then to the solution was injected with a syringe 1.5 mL of water containing 0.60 g of NaOH (15 mmol). 24 h later, the mixture was poured into a saturated aqueous $NaHCO_3$ solution (50 mL), and was extracted with ethyl acetate (3× 50 mL). The combined organic phases were washed with brine (6× 100 mL), dried over Na_2SO_4, and concentrated under reduced pressure on a rotary evaporator. The thus obtained residual was treated with silica gel column chromatography (with petroleum ether and ethyl acetate (15:1) as effluent) to give **1**.[23]

General procedure for the reaction of compounds 1 with Togni's reagent

A mixture of **1** (0.5 mmol), Togni's reagent (2.0 mmol, 632 mg) and CuI (0.05 mmol, 9.5 mg) in 5 mL toluene was stirred at 80 °C (in an oil bath) under an argon atmosphere for 16 h. The reaction mixture was then cooled to room temperature, and was poured into a saturated aqueous K_2CO_3 solution (10 mL). The aqueous phase was extracted with ethyl acetate (3× 10 mL), and the combined organic layers were washed sequentially with saturated aqueous K_2CO_3 solution (10 mL) and brine, and then dried over Na_2SO_4. The solvent was evaporated under reduced pressure on a rotary evaporator, and the residual was treated with silica gel column chromatography (with petroleum ether and ethyl acetate (10:1) as effluent unless otherwise specified) to give product **2** (or **3g**).

General procedure for the reaction of compounds 1 with Zhdankin's reagent

A mixture of **1** (0.5 mmol), Zhdankin's reagent (1.0 mmol, 289 mg) and CuI (0.05 mmol, 9.5 mg) in 5 mL toluene was stirred at 60 °C (in an oil bath) under an argon atmosphere until **1** was consumed completely as indicated by TLC (4-16 h). The reaction mixture was then cooled to room temperature, and was poured into a saturated aqueous K_2CO_3 solution (10 mL). The aqueous phase was extracted with ethyl acetate (3× 10 mL), and the combined organic layers were washed sequentially with saturated aqueous K_2CO_3 solution (10 mL) and brine, and then dried over Na_2SO_4. The solvent was

evaporated under reduced pressure on a rotary evaporator, and the residual was purified by silica gel column chromatography (with petroleum ether and ethyl acetate (5:1) as effluent) to give product **4** and **5**.

Representative characterization data

2-Azido-*N*-benzyl-*N*-phenylacrylamide (1a)

Yellow oil: R_f = 0.45 (petroleum ether : ethyl acetate = 5:1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.30–7.20 (m, 8H), 7.01–6.99 (m, 2H), 4.97 (s, 2H), 4.92 (d, *J* = 2.0 Hz, 1H), 4.88 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm $CDCl_3$): 164.0, 141.9, 140.0, 136.4, 129.1, 128.4, 128.3, 127.5, 127.4, 126.9, 106.4, 53.4; FT-IR (KBr, cm^{-1}): 2107, 1652.5; HRMS (ESI): calcd. for $C_{16}H_{14}N_4O$+H = 279.1248, found 279.1245.

2-Azido-*N*-benzyl-*N*-(4-fluorophenyl)acrylamide (1b)

Yellow solid: m.p. = 41–42 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.27–7.24 (m, 3H) , 7.20–7.18 (m, 2H), 6.96 (d, *J* = 6.4 Hz, 4H), 4.97 (s, 1H), 4.93 (s, 2H), 4.92 (d, *J* = 2.0 Hz, 1H) ; ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 164.0, 161.4 (d, *J* = 247 Hz), 139.9, 137.7, 136.1, 128.9, 128.8, 128.6, 128.5, 128.4, 127.7, 116.1, 115.9, 106.4, 53.5; FT-IR (KBr, cm^{-1}): 2108.8, 1642.4; ESI-HRMS: m/z calcd for $C_{16}H_{13}FN_4O$+H = 297.1152, found 297.1143.

2-Azido-*N*-benzyl-*N*-(4-chlorophenyl)acrylamide (1c)

Colorless oil: R_f = 0.45 (petroleum ether : ethyl acetate = 5:1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.29–7.24 (m, 5H), 7.20–7.18 (m, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 5.00 (d, *J* = 2.0 Hz, 1H), 4.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 164.0, 140.5, 140.0, 136.2, 133.4, 129.4, 128.6, 128.5, 128.4, 127.7, 106.6, 53.5; FT-IR (KBr, cm^{-1}): 2107.8, 1652.4; ESI-HRMS: m/z calcd for $C_{16}H_{13}ClN_4O$+H = 313.0856, found 313.0849.

2-Azido-*N*-benzyl-*N*-(4-bromophenyl)acrylamide (1d)

Colorless oil: R_f = 0.53 (petroleum ether : ethyl acetate = 5:1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.38 (d, *J* = 8.4 Hz, 2H), 7.25–7.18 (m, 3H), 7.18–7.16 (m, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.01 (d, *J* = 2.4 Hz, 1H), 4.95 (d, *J* = 2.0 Hz, 1H), 4.94 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 152.7, 137.2, 135.0, 134.0, 133.7, 133.6, 132.5, 129.3, 128.4, 126.9, 117.7, 116.4, 113.6, 46.7; FT-IR (KBr, cm^{-1}): 2109.8, 1646.4; ESI-HRMS: m/z calcd for $C_{16}H_{13}BrN_4O$+H = 357.0351, found 357.0344.

1-Benzyl-3-(2,2,2-trifluoroethyl)quinoxalin-2(1*H*)-one (2a)

White solid: m.p. = 109–112 °C (recrystallized from petroleum ether and CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.90 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.47 (dt, *J* = 1.6 Hz, 8.0 Hz, 1H), 7.33–7.22 (m, 7H), 5.51 (s, 2H), 3.90 (q, *J* = 10.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.6, 150.7, 134.8, 132.7, 132.7, 131.2, 130.7, 129.0, 127.8, 126.8, 125.1, 124.0, 114.5, 46.2, 37.4 (q, *J* = 30 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz, δ ppm): -63.66 (dt, *J*= 3.0, 12.0 Hz); ESI-HRMS: m/z calcd for $C_{17}H_{13}F_3N_2O$+H = 319.1058, found 319.1051.

1-Benzyl-6-fluoro-3-(2,2,2-trifluoroethyl)quinoxalin-2(1*H*)-one (2b)

White solid: m.p. = 108–110 °C (recrystallized from petroleum ether and CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.61–7.59 (m, 1H), 7.34–7.27 (m, 3H), 7.24–7.20 (m, 4H), 5.50 (s, 2H), 3.91 (q, *J* = 10.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 158.7 (d, *J* = 253 Hz), 154.3, 152.3, 152.2, 134.6, 133.2, 133.1, 129.4, 129.3, 129.1, 128.0, 126.8, 126.7, 126.3, 123.6, 119.0, 118.9, 116.1, 115.9, 115.8, 115.7, 46.4, 37.5 (q, *J* = 30 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz, δ ppm): -62.81 (t, *J* = 10.0 Hz, 3F), 118.03–-118.08 (m, 1F); ESI-HRMS: m/z calcd for $C_{17}H_{12}F_4N_2O$+H = 337.0964, found 337.0956.

1-Benzyl-6-chloro-3-(2,2,2-trifluoroethyl)quinoxalin-2(1*H*)-one (2c)

Yellow solid: m.p. = 149–151 °C (recrystallized from petroleum ether and CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.90 (d, *J* = 2.0 Hz, 1H), 7.82 (d, *J* = 2.0 Hz, 0.05H), 7.41 (dd, *J* = 2.4 Hz, *J* = 8.8 Hz, 1 H), 7.34–7.26 (m, 3H), 7.20–7.19 (m, 3H), 5.47 (s, 2H), 4.67 (s, 0.10H), 3.89 (q, *J* = 10.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.2, 152.1, 134.5, 133.1, 131.4, 131.1, 130.0, 129.4, 129.0, 128.0, 126.7, 126.3, 123.6, 115.7, 46.3, 37.6 (q, *J* = 30 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz, δ ppm): -62.81 (t, *J* = 12.0 Hz); ESI-HRMS: m/z calcd for $C_{17}H_{12}ClF_3N_2O$+H = 353.0669, found 353.0659.

1-Benzyl-6-bromo-3-(2,2,2-trifluoroethyl)quinoxalin-2(1*H*)-one (2d)

White solid: m.p. = 118–121 °C (recrystallized from petroleum ether and CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.06 (d, *J* = 2.0 Hz, 1H), 7.54 (dd, *J* = 2.0 Hz, 9.2 Hz, 1H), 7.30 (m, 3H), 7.20–7.19 (m, 2H), 7.14 (d, *J* = 8.8 Hz, 1H), 5.47 (s, 2H), 3.90 (q, *J* = 10.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.2, 152.1, 152.0, 134.4, 134.8, 133.4, 133.0, 131.8, 129.1, 128.6, 128.5, 128.0, 126.7, 126.3, 123.5, 116.6, 116.0, 46.3, 37.4 (q, *J* = 30 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz, δ ppm): -63.53 (t, *J* = 12.4 Hz); ESI-HRMS: m/z calcd for $C_{17}H_{12}F_3IN_2O$+H = 445.0025, found 445.0021.

3-(Azidomethyl)-1-benzylquinoxalin-2(1*H*)-one (4a)

White solid:m.p. = 61–63 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.96 (dd, *J* = 2.0 Hz, *J* = 8.0 Hz, 1H), 7.48 (dt, *J* = 2.0 Hz, *J* = 8.0 Hz, 1H), 7.37–7.27 (m, 5H), 7.25–7.23 (m, 2H), 5.52 (s, 2H), 4.67 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.2, 134.8, 132.7, 130.8, 130.6, 129.0, 127.8, 126.8, 124.0, 114.5, 51.8, 45.9; ESI-HRMS: m/z calcd for $C_{16}H_{13}N_5O$+Na = 314.1012, found: 314.1007.

4-Benzyl-3-oxo-3,4-dihydroquinoxaline-2-carbonitrile (5a)

Brown solid: m.p. = 175–178 °C; ^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 7.96 (d, *J* = 10.0 Hz, 1H), 7.66 (t, *J* = 10.0 Hz, 1H), 7.45–7.25 (m, 7H), 5.53 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 153.1, 134.6, 133.9, 133.7, 133.4, 133.1, 131.9, 129.1, 128.2, 127.0, 125.0, 115.0, 114.0, 46.5; HRMS (ESI): calcd. for $C_{16}H_{11}N_3O$+Na = 284.0794, found: 284.0798.

3-(Azidomethyl)-1-benzyl-6-fluoroquinoxalin-2(1*H*)-one (4b)

Yellow oil: R_f = 0.37 (petroleum ether : ethyl acetate = 3:1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.65 (dd, *J* = 2.4 Hz, *J* = 8.4 Hz, 1H), 7.35–7.28 (m , 3H), 7.24–7.21 (m, 4H), 5.50 (s, 2H), 4.66 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 158.7 (d, *J* = 244 Hz), 155.8, 153.8, 134.5, 133.3, 133.1, 129.2, 129.1, 129.0, 128.0, 126.7, 118.8, 116.1, 115.8, 115.8, 115.7, 51.7, 46.1; HRMS (ESI): calcd. for $C_{16}H_{12}FN_5O$+Na = 332.0918, found 332.0923.

4-Benzyl-7-fluoro-3-oxo-3,4-dihydroquinoxaline-2-carbonitrile (5b)

Light yellow solid: m.p. = 205–208 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.65 (dd, *J* = 2.4 Hz, *J* = 8.0 Hz, 1H), 7.42–7.33 (m , 5H), 7.31–7.21 (m, 2H), 5.52 (s, 2H) ; ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 158.9 (d, *J* = 246 Hz), 152.7, 135.3, 133.7, 133.6, 133.5, 130.2, 129.3, 129.1, 128.4, 126.9, 126.8, 122.9, 122.6, 117.0,

116.7, 116.4, 116.4, 113.7, 46.8; HRMS (ESI): calcd. for $C_{16}H_{10}FN_3O$+Na = 302.0700, found 302.0702.

3-(Azidomethyl)-1-benzyl-6-chloroquinoxalin-2(1*H*)-one (4c)

White solid: m.p. = 128−130 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.13 (d, *J* = 1.6 Hz, 1H), 7.41 (dd, *J* = 2.4 Hz, *J* = 8.8 Hz, 1H), 7.34−7.26 (m , 3H), 7.22−7.20 (m, 3H), 5.48 (s, 2H), 4.64 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 155.7, 153.8, 134.4, 133.1, 131.2, 130.8, 129.8, 129.4, 129.1, 128.0, 126.7, 115.7, 57.6, 46.0; HRMS (ESI): calcd. for $C_{16}H_{12}ClN_5O$+Na = 348.0623, found 348.0626.

4-Benzyl-7-chloro-3-oxo-3,4-dihydroquinoxaline-2-carbonitrile (5c)

Yellow solid: m.p. = 195−198 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.95 (d, *J* = 2.4 Hz, 1H), 7.58 (dd, *J* = 2.4 Hz, *J* = 9.2 Hz, 1H), 7.37−7.30 (m, 4H), 7.25−7.23 (m, 2H), 5.50 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 152.7, 135.1, 134.5, 133.6, 133.4, 132.0, 130.9, 130.6, 129.3, 128.4, 126.9, 116.2, 113.7, 46.8; HRMS (ESI): calcd. for $C_{16}H_{10}ClN_3O$+Na = 318.0405, found 318.0413.

4-Benzyl-7-bromo-3-oxo-3,4-dihydroquinoxaline-2-carbonitrile (5d)

Yellow solid: m.p. = 197−200 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.10 (d, *J* = 2.4 Hz, 1H), 7.71 (dd, *J* = 2.4 Hz, *J* = 8.8 Hz, 1H), 7.36−7.30 (m, 3H), 7.27−7.23 (m, 3H), 5.50 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 152.7, 137.2, 135.0, 134.0, 133.7, 133.6, 132.5, 129.3, 128.4, 126.9, 117.7, 116.4, 113.6, 46.7; HRMS (ESI): calcd. for $C_{16}H_{10}BrN_3O$+Na = 363.9879, found 363.9882.

Acknowledgements

The authors thank the National Natural Science Foundation of China (No. 21372108) for financial support.

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