Advanced Synthesis & Catalysis

DOI: 10.1002/adsc.201500305

tert-Butyl Hydroperoxide and Tetrabutylammonium Iodide-Promoted Free Radical Cyclization of α-Imino-*N*-arylamides and α-Azido-*N*-arylamides

Dianjun Li,[a] Tonghao Yang,[a] Hailin Su,[a] and Wei Yu[a,*]

[a] State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, People's Republic of China
Fax: +86-931-891-2582; e-mail: yuwei@lzu.edu.cn

Received: March 27, 2015; Revised: April 25, 2015; Published online: July 29, 2015

Abstract: The oxidizing system of *tert*-butyl hydroperoxide (TBHP) and tetrabutylammonium iodide (TBAI) is capable of generating α-(arylaminocarbonyl)iminyl radicals from ethyl 2-(*N*-arylcarbamoyl)-2-iminoacetates. These iminyl radicals preferably undergo intramolecular *ipso* attack on the benzene ring to give azaspirocyclohexadienyl radicals, which are readily captured by molecular oxygen under an oxygen atmosphere to yield azaspirocyclohexadienones. In the absence of oxygen, the reaction affords quinoxalin-2-one products. This oxidizing system is also effective to convert α-aryl-α-azido-*N*-arylamides to the corresponding iminyl radicals under basic conditions (sodium *tert*-butoxide, *t*-BuONa), and the subsequent cyclization of these iminyl radicals results in the formation of azaspirocyclohexadienone products in high yields under an oxygen atmosphere. Plausible mechanisms are proposed to rationalize the experimental results, and factors influencing the reactions are discussed.

Keywords: (*N*-arylcarbamyl)-2-iminoacetates; α-azido-*N*-arylacetamide; *tert*-butyl hydroperoxide; iminyl radicals; oxidative cyclization; tetrabutylammonium iodide

Introduction

The radical chemistry of organic azides has proved to be very useful in organic synthesis.[1] Apart from the radical azidation methods,[2,3] organic azides can undergo radical reactions of other patterns: by reaction with carbon[4] or hetero-centered radicals[5] or reduction by low valent-metal reductants,[1b] they can also be converted to aminyl radicals; the α-azidyl carbon radicals, on the other hand, can readily extrude a nitrogen molecule to afford iminyl radicals.[6–8] Thus, organic azides provide a convenient source for other nitrogen-centered radicals. Nonetheless, despite the importance of these nitrogen-centered radicals in the synthesis of nitrogen heterocycles,[9] these significant features of azides have not been fully explored.

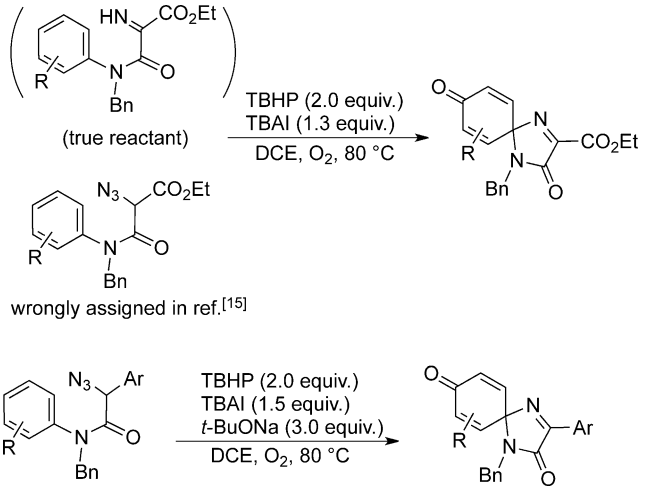
This is especially the case when one considers the potential usefulness of azides as the iminyl radical source. Only recently has it begun to receive attention from the synthetic point of view. Studies toward this end were firstly reported by Spagnolo et al.,[6] who investigated the reactions of α-(aminocarbonyl)iminyl radicals derived from α-azido-*o*-iodoanilides.[6b] In that study, the generation of the iminyl radical was realized through 1,5-hydrogen transfer from the α-carbon to the phenyl radical (formed under standard tin hydride conditions) and dinitrogen expulsion. The authors found that these α-(aminocarbonyl)iminyl radicals exhibit a strong tendency to fragment to nitriles, and meanwhile minor amounts of quinoxalinone products were generated as a result of iminyl radical cyclization. Later on, Chiba et al. reported an elegant copper-catalyzed aerobic oxidative cyclization of α-azido-*N*-arylamides, which produced azaspirocyclohexadienones in good yields.[10] In this reaction, the copper-mediated iminyl radical is firstly generated,[9f,11] which then undergoes intramolecular *ipso* attack on the benzene ring to form the C–N bond. Recently, Zhang et al. reported an *N*-bromosuccinimide (NBS)-mediated cyclization of 2-azido-*N*-arylacetamides.[12] This process also entails the α-(aminocarbonyl)iminyl radical as a key intermediate; its subsequent cyclization yields both the quinoxalin-2-one and spirocyclic products, the ratio of which is largely dependent on the electronic nature of substituents at the benzene ring.

It can be seen from these published results that while organic azides have proved to be valuable iminyl radical precursors, the related studies are still limited. As far as α-(aminocarbonyl)iminyl radicals

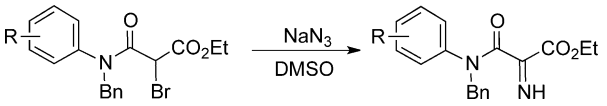
are concerned, there are several issues that need to be addressed. Firstly, their reactivity, seemingly varying from case to case according to the available examples, should be further explored. As demonstrated by the aforementioned recent studies, the intramolecular attack of an iminyl radical center on the *N*-phenyl ring can take place at both *ipso* and *ortho* positions, but factors influencing the selectivity have not been clarified. Secondly, the role played by oxygen needs to be addressed. It is possible that molecular oxygen has a big influence on the reaction outcome. Thirdly, considering the synthetic usefulness of iminyl radicals, new protocols are highly desirable to enhance the general applicability of the azide-based/iminyl radical-mediated methodology.

During our previous investigations on the oxidative coupling involving 1,3-dicarbonyl compounds, we found that the reagent combination of *tert*-butyl hydroperoxide (TBHP) and tetrabutylammonium iodide (TBAI) could effect the C–N oxidative coupling of 2-aminopyridines with β-keto esters, and the reaction afforded imidazo[1,2-*a*]pyridines in moderate to good yields.[13] Following this work, we reported that α-substituted β-acetylamides could be converted to α-keto amides *via* oxidative C–C bond cleavage by treatment with $CuCl_2/BF_3{\cdot}OEt_2$/TBHP under an oxygen atmosphere.[14] On the basis of these results, we hoped that the TBHP-based oxidizing systems might be used to turn 2-azido-*N*-phenylacetamides into α-(aminocarbonyl)iminyl radicals under metal-free conditions. In this way, the iminyl radicals would be generated under both oxygen and argon atmospheres, and thus the effect of oxygen could be evaluated.

Our subsequent study demonstrated that the desired transformations can be really achieved by using the oxidizing system of TBHP/TBAI, and the results were revealed in a recent paper (Scheme 1).[15] However, we soon found that one group of the reactants,



Scheme 1. Results revealed in ref.[15]



Scheme 2. Formation of 2-(*N*-arylcarbamoyl)-2-iminoacetates

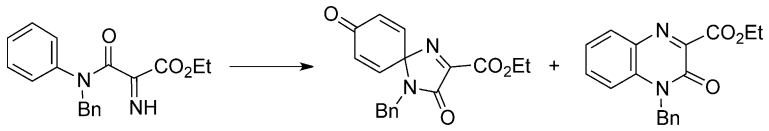
which were assigned as α-ethoxycarbonyl-α-azido-*N*-phenylacetamides in this paper, are actually ethyl 2-(*N*-arylcarbamoyl)-2-iminoacetates that resulted from the denitrogenation of the former during the preparation (Scheme 2, see the Supporting Information). The imino compounds are the proposed intermediates towards the cyclization products. Due to these mistakes,[15] we retracted this paper at the agreement of the Editorial Office, and reworked it extensively. Herein we wish to present the corrected version of this report.

Results and Discussion

At the initial stage of this investigation, we chose compound 2-(*N*-benzyl-*N*-phenylcarbamoyl)-2-iminoacetate (**1a**) as the model compound, and subjected it to TBHP under a variety of conditions. The results are summarized in Table 1, from which it can be seen that the reagent combination of TBHP and TBAI is capable of oxidizing **1a**, whereas using TBHP alone is ineffective (Table 1, entry 1). When **1a** was treated with 1.4 equiv. of TBAI and 1.9 equiv. of TBHP (either in water or in decane) in acetonitrile under an air atmosphere, **2a** and **3a** were formed as the major products, the ratio of which was dependent on the reaction temperature (entries 2–4, and 7). The yield of **2a** could be increased when the reaction was carried out under an O_2 atmosphere (O_2 balloon) (entries 6, 9 and 10). On the other hand, when the reaction was carried out under an argon atmosphere, only a tiny amount of **2a** was obtained, but the yield of **3a** was still moderate (entries 5 and 8). The reaction was very slow when only a catalytic amount of TBAI was used (entry 11), and it did not happen in the absence of TBHP (entry 15). Using H_2O_2 as oxidant in place of TBHP failed to effect the reaction (entry 12). On the other hand, when TBAI was replaced by molecular iodine, a complex mixture was formed (entry 13). The reaction exhibited a large solvent effect: it did not take place in toluene (entry 14), but the yield of **2a** was remarkably improved in 1,2-dichloroethane (DCE) under an O_2 atmosphere (entries 19 and 20). It is interesting to see that with DCE as the solvent, **2a** was formed in roughly the same yield as **3a** even under an argon atmosphere (entry 16).

These results can be interpreted with the mechanism shown in Scheme 3. The reaction is initiated by the oxidation of **1a** to give iminyl radical **A**. The

Table 1. Screening of reaction conditions for the reaction of **1**.[a]



Entry	Oxidant (equiv.)	Additive (equiv.)	Atmosphere	Solvent (Temp.)	Reaction time [h]	Product (Yield [%])[b]
1	TBHP[c] (1.9)	none	air	CH_3CN (100 °C)	2.5	N.R.[e]
2	TBHP[c] (1.9)	TBAI (1.4)	air	CH_3CN (100 °C)	2.5	**2a** (28), **3a** (33)
3	TBHP[c] (1.9)	TBAI (1.4)	air	CH_3CN (80 °C)	2.5	**2a** (41), **3a** (25)
4	TBHP[c] (1.9)	TBAI (1.4)	air	CH_3CN (50 °C)	4	**2a** (14), **3a** (40)
5	TBHP[c] (1.9)	TBAI (1.4)	Ar	CH_3CN (100 °C)	3	**2a** (3), **3a** (46) + mixture
6	TBHP[c] (1.9)	TBAI (1.4)	O_2	CH_3CN (80 °C)	2.5	**2a** (56), **3a** (20)
7	TBHP[d] (1.9)	TBAI (1.4)	air	CH_3CN (80 °C)	3	**2a** (47), **3a** (21)
8	TBHP[d] (1.9)	TBAI (1.4)	Ar	CH_3CN (80 °C)	3	**2a** (trace), **3a** (38) + mixture
9	TBHP[d] (1.9)	TBAI (1.4)	O_2	CH_3CN (80 °C)	2.5	**2a** (66), **3a** (15)
10	TBHP[d] (1.9)	TBAI (0.9)	O_2	CH_3CN (80 °C)	2.5	**2a** (65), **3a** (13)
11	TBHP[d] (1.9)	TBAI (0.2)	O_2	CH_3CN (80 °C)	3	**2a** (14), **3a** (5)[f]
12	H_2O_2 (30 %) (1.9)	TBAI (1.4)	O_2	CH_3CN (80 °C)	4	N.R.[e]
13	TBHP[d] (1.9)	I_2 (1.4)	O_2	CH_3CN (80 °C)	4	mixture
14	TBHP[d] (1.9)	TBAI (1.4)	O_2	toluene (75 °C)	4	N.R.[e]
15	none	TBAI (1.4)	air	CH_3CN (80 °C)	6	N.R.[e]
16	TBHP[d] (1.9)	TBAI (1.4)	Ar	DCE (80 °C)	2.5	**2a** (42), **3a** (40)
17	TBHP[d] (1.9)	TBAI (1.4)	air	DCE (r.t.)	24	**2a** (11), **3a** (trace)[g]
18	TBHP[d] (1.9)	TBAI (1.4)	air	DCE (80 °C)	2.5	**2a** (52), **3a** (32)
19	***TBHP[d] (1.9)***	***TBAI (1.2)***	***O_2***	***DCE (80 °C)***	***1.5***	***2a (85), 3a (trace)***
20	TBHP[d] (1.9)	TBAI (0.9)	O_2	DCE (80 °C)	1.5	**2a** (83), **3a** (trace)
21	TBHP[d] (1.1)	TBAI (1.2)	O_2	DCE (80 °C)	2	**2a** (67), **3a** (trace)

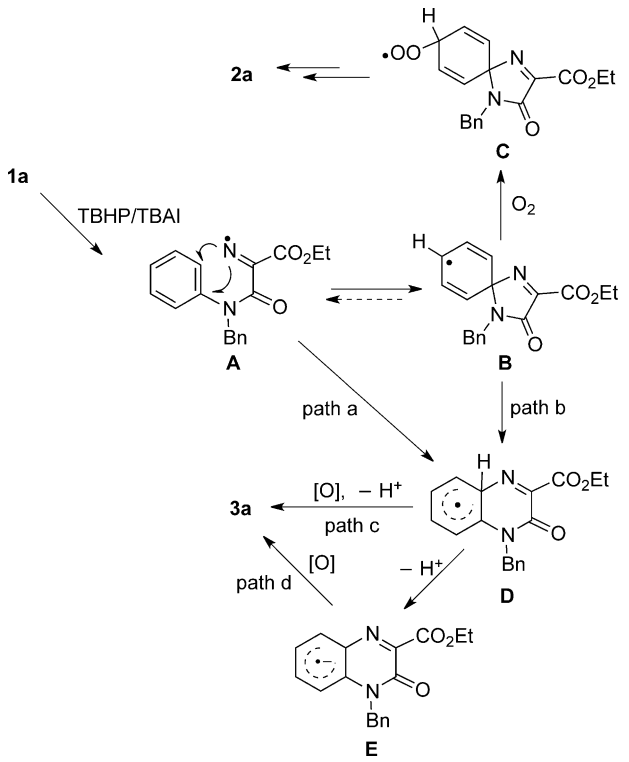
[a] The reaction was performed in a solution of 0.1 M **1a**.
[b] Isolated yield.
[c] 70% in water.
[d] *Ca.* 5.5 M in decane.
[e] No reaction.
[f] 70% starting material recovered.
[g] 75% starting material recovered.

latter undergoes facile *ipso*-5-*exo* cyclization to afford radical **B**. Under an oxygen atmosphere, **B** is captured by oxygen to yield peroxy radical **C**, from which **2a** is generated. This reaction pattern is consistent with the previously reported studies.[10,11c,12] When the reaction proceeds under an argon atmosphere, radical **B** undergoes 1,2-migration of the iminyl moiety to yield radical **D**, or ring opening to give back iminyl radical **A**, and from **D** quinoxalin-2-one **3a** is eventually formed.

Two possible pathways are available for the formation of radical **D**: the first is the intramolecular *ortho*-attacking cyclization of iminyl radical **A** (path a, Scheme 3); the second involves the 1,2-migration of the iminyl group from **B** (path b, Scheme 3). Under both circumstances, **B** is formed in the first place. That **2a** was formed predominantly under an oxygen atmosphere clearly proves this point.

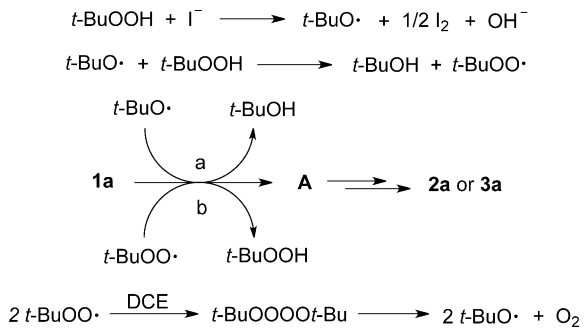
Previous work by Spagnolo et al. demonstrates that α-(phenylaminocarbonyl)iminyl radicals like **A** are inclined to fragment to nitriles.[6b] That explains why the yield of quinoxalin-2-one product is quite low in their case. This tendency of fragmentation has also been demonstrated by Chiba's work on the copper-catalyzed reaction of α-azido carbonyl compounds.[16] In the present case, the fragmentation of radical **A** is much less favored compared with the intermolecular *ipso* attack, and thus **A** was transformed to **B** preferentially. In an environment saturated with oxygen, **B** would be captured rapidly by oxygen to give eventually **2a** in high yield. However, in the absence of oxygen, the transformation from **B** to **A** becomes reversible, and the fragmentation will have a chance to compete with other pathways. Therefore, when the reaction was carried out under argon atmosphere, the yield of **3a** was considerably lower than that of **2a** in the presence of oxygen.

The transformation from **A** to **3a** through **D** is a typical homolytic aromatic substitution (HAS) reaction.[17] For the formation of **3a**, a hydrogen atom must be removed from **D**, a process that might be realized *via* oxidation followed by deprotonation (path



Scheme 3. Proposed mechanism for the TBHP/TBAI-promoted reaction of **1a**.

c, Scheme 3). Very recently, Studer and Curran proposed a different scenario to rationalize the homolytic aromatic substitution under basic conditions. Their study indicates that the cyclohexadienyl radicals like **D** formed in the HAS reactions are quite acidic, and can be readily removed with a base.[18] According to this base-promoted homolytic aromatic substitution (BHAS) mechanism, it is possible that the conversion of **D** to **3a** firstly involves a deprotonation step to afford radical anion **E**; the latter is then oxidized to **3a** (path d, Scheme 3). As can be seen in Scheme 4, the reaction of TBHP and iodide ion produces hydroxide ion, which can promote the deprotonation step.



Scheme 4. Proposed mechanism for the TBHP/TBAI-mediated oxidation of **1a** to iminyl radical **A**.

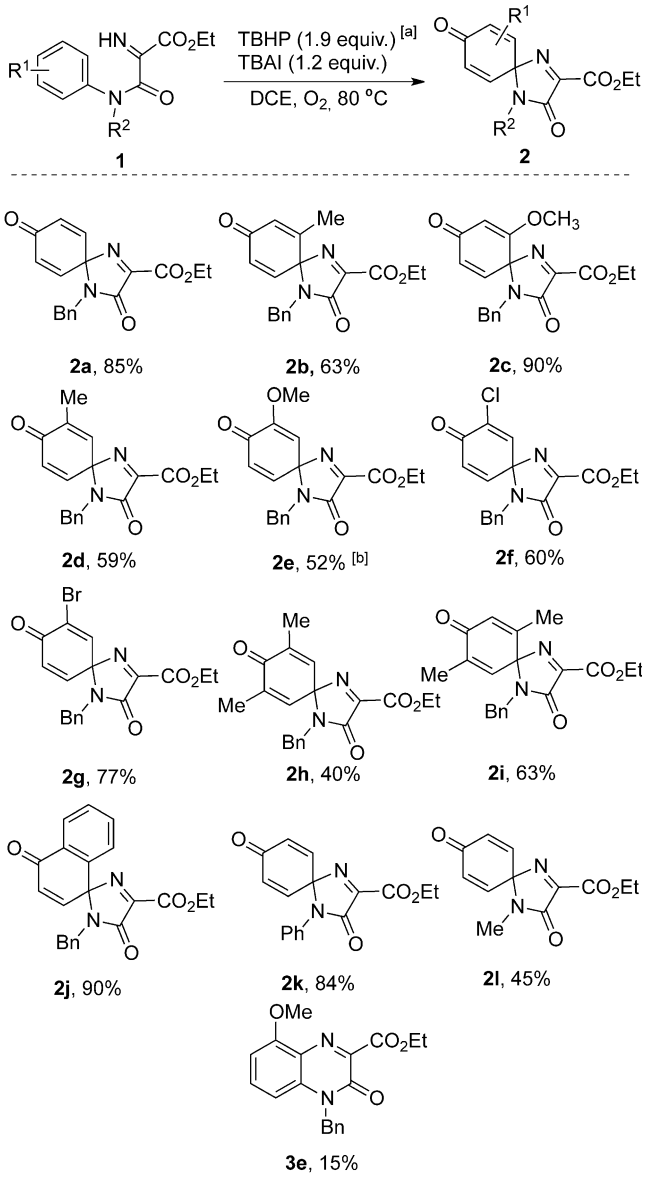
The oxidizing system of TBHP and TBAI has recently been extensively applied to various types of oxidative transformations.[19] From the mechanistic point of view, its oxidizing capacities generally fall into two categories: the first involves the *in situ* generated *tert*-butoxy radical; the second involves the hypervalent iodine species $[(n\text{-}Bu)_4N]^+IO^-$ and $[(n\text{-}Bu)_4N]^+IO_2^-$.[20] In the present cases, we assume that these hypervalent iodines are less likely to be the active oxidants since the combination of H_2O_2 (30%) and TBAI, which is also capable of generating hypervalent iodine species, is ineffective here (Table 1, entry 12).

Consequently, a mechanism is proposed to account for the formation of iminyl radical **A** from **1a** (Scheme 4). We believe that the *tert*-butoxy radical is the active oxidant in the present reaction system. Besides the *tert*-butoxy radical, the *tert*-butyl peroxyl radical probably also acts as the oxidant since it can be generated from *tert*-butoxy radical and TBHP.[21] That **2a** was generated together with **3a** in DCE even under an argon atmosphere supports this point: *in situ* generation of O_2 probably occurs *via* dimerization of the *tert*-butyl peroxyl radical followed by O–O cleavage. The oxidation takes place probably *via* a single electron transfer between **1a** and *tert*-butoxyl radical (or *tert*-butyl peroxyl radical).

To explore the scope of the reaction with regard to the substituent effect, the optimal conditions for the formation of **2a** (Table 1, entry 19) were applied to a variety of substituted α-imino-*N*-arylacetamides **1**, and the results are illustrated in Scheme 5, Scheme 6 and Scheme 7. For the reactions of *ortho*- and *meta*-substituted substrates **1**, azaspirocyclohexadienones **2** were generated predominantly, the yields of which varied according to the substituents. Besides the substituent at the phenyl ring, that at the amido nitrogen atom also influenced the yield of **2**. As such, the yield of **2l** was considerably lower than that for its *N*-benzyl or *N*-phenyl substituted counterpart (Scheme 5).

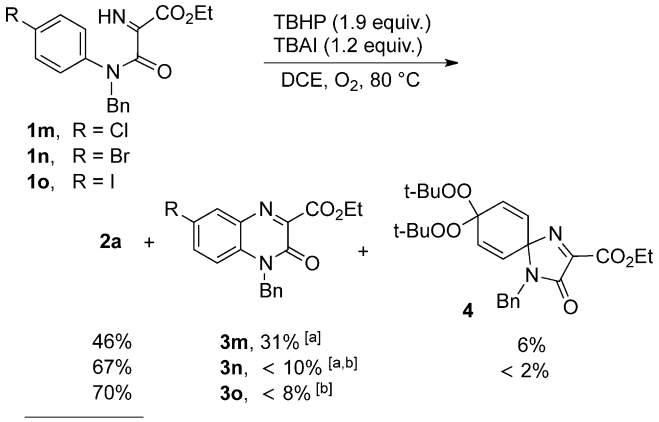
When substrates incorporating a substituent at the *para* position were subjected to the current conditions, mixed results were obtained after reaction: for the reaction of **1m**–**1o**, the major product was **2a**, accompanied by a minor amount of **3m**–**3o** (Scheme 6). In the cases of **1m** and **1n**, a tiny amount of di-*tert*-butylperoxy-substituted azaspirocyclohexadienyl product **4** was also obtained. On the other hand, when the substrate was **1p** or **1q**, the reaction afforded a mixture of mono-*tert*-butylperoxy-attached azaspirocyclic product **4′** and quinoxalin-2-one **3** (Scheme 7) (the relative configuration of **4′** was undetermined).

The formation of compound **4** and **4′** can be accounted for with the mechanisms shown in Scheme 8: In path (a), the azaspirocyclic radical **B** derived from the corresponding substrate is transformed to perox-



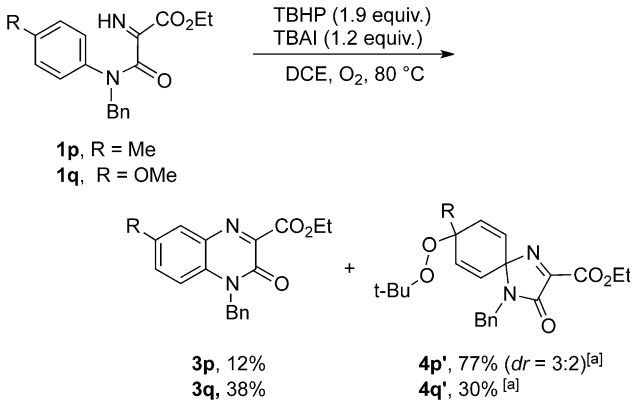
[a] The reaction was carried out on a scale of 0.53–0.54 mmol. Isolated yield.
[b] Besides **2e**, **3e** was also obtained in a yield of 15%.

Scheme 5. TBHP and TBAI-mediated oxidative cyclization of **1** under oxygen atmosphere.



[a] Obtained as a mixture of **3** and **4.**
[b] Could not be obtained in pure form.

Scheme 6. Reactions of *para*-substituted **1m**–**1o**.



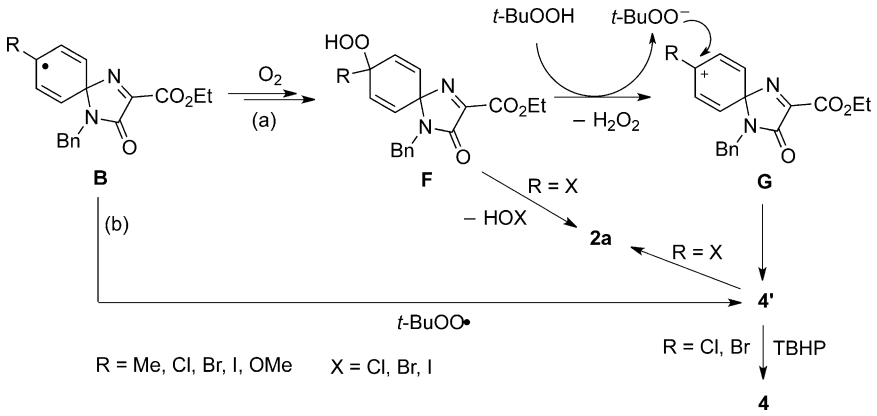
[a] The relative configuration is undetermined.

Scheme 7. Reactions of *para*-substituted **1p** and **1q**.

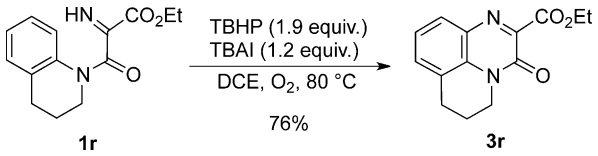
ide **F** under an oxygen atmosphere, which subsequently undergoes elimination of HOO^- to afford carbocation **G**. The latter is captured by *t*-$BuOO^-$ to yield **4′**. When R is a halogen atom, a competitive elimination from peroxide **F** and **4′** takes place, and thus **2a** is generated. In the cases of **1m** and **1n**, a tiny amount of **4′** undergoes nucleophilic substitution with TBHP to afford compound **4**. Similar elimination products have been reported by Zhang et al.[12] As an alternative to this mechanism, **4′** can result from the trapping of **B** by *tert*-butyl peroxyl radical. The *tert*-butyl peroxyl radical has a rather long lifetime,[22] and therefore is capable of capturing intermediate **B** (persistent radical effect) to give **4′** [mechanism (b)]. Similar coupling reactions as steered by the persistent radical effect have been well documented in the literature.[23]

When compound **1r** was treated with TBHP and TBAI under an oxygen atmosphere, **3r** was generated in 76% yield (Scheme 9). This result is consistent with the anticipation that the intramolecular *ipso*-attack in this particular case was difficult due to the unfavorable conformational effect posed by the tetrahydroquinoline ring, while the formation of a **D**-like radical became favorable.

As indicated in Table 1, apart from **2a**, quinoxalin-2-one **3a** could also form from the oxidation of **1a**, and compound **3a** was obtained almost exclusively when the reaction was carried out in CH_3CN under an argon atmosphere (Table 1, entry 5). To further explore the influence of the substituent, we next applied these conditions to several substituted substrates **1**, and the results are illustrated in Table 2. Here again



Scheme 8. Proposed mechanism for the formation of **2a**, **4** and **4′** in the reactions of **1m**–**1q**.

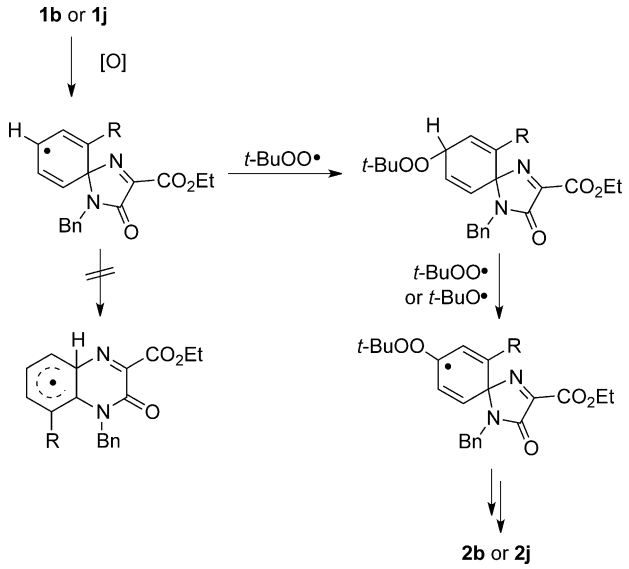


Scheme 9. Reaction of **1r** under an oxygen atmosphere.

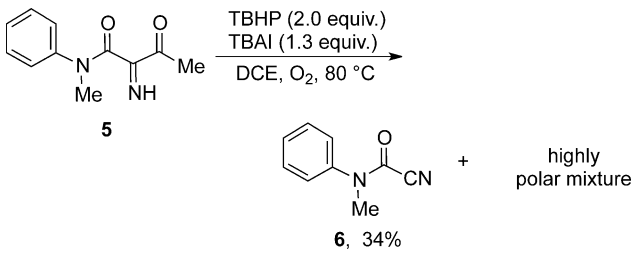
the position of the substituent on the *N*-phenyl ring exerted a huge influence on the composition of the products, which varied depending on the substitution patterns. For the reactions of compound **1d** and **1f**, the major products were the corresponding quinoxalin-2-ones **3d** and **3f** as a mixture of regio-isomers, along with a minor amount of **2d** and **2f**. The quinoxalin-2-one-forming cyclization exhibited *ortho* selectivity in both cases, which is consistent with the previous reports dealing with attack of carbon radicals on the substituted benzene ring.[24]

In contrast to this result, when compound **1b** and **1j** were used, only **2b** and **2j** were obtained after reaction, indicating that the *ortho*-attack is hampered by the presence of an *ortho*-substituent. The formation of **2b** and **2j** can be accounted for with the mechanism shown in Scheme 10. On the other hand, the reaction of *para*-substituted **1p** and **1q** delivered a mixture of **3** and **4′**, while the reaction of **1m–1o** produced **2a** as well as **3**. All these results are in accordance with the mechanism shown in Scheme 3 and Scheme 8.

Although this protocol is effective for the reaction of compounds **1**, it failed to produce similar results when the ethyloxycarbonyl group was replaced by an acetyl group (compound **5**). In the latter case, the reaction delivered compound **6** in 34% yield (Scheme 11). The generation of **6** is consistent with the notion that iminyl radicals are susceptible to fragmentation, and at the same time reflects the strong influence of the α-substituent on the reactivity of iminyl radicals.



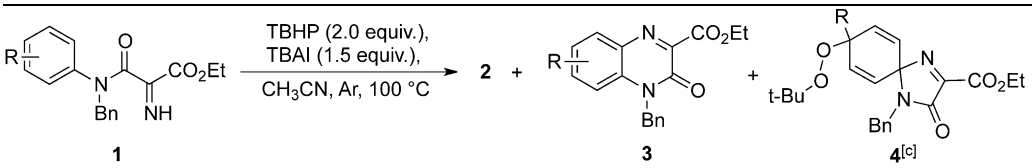
Scheme 10. Proposed mechanism for the formation of **2** under an argon atmosphere.



Scheme 11. The result with **5** as the substrate.

We next examined the applicability of this TBHP/TBAI system to the reaction of α-aryl-α-azido-*N*-arylamides **7**. As demonstrated by Chiba et al.,[10] α-aryl-α-azido-*N*-arylamides can be transformed to the corresponding iminyl radicals through the ketimine intermediates under copper-mediated oxidative conditions. We anticipated that the current metal-free protocols

Table 2. Reaction of **1** under an argon atmosphere.[a]



1

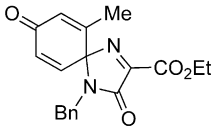
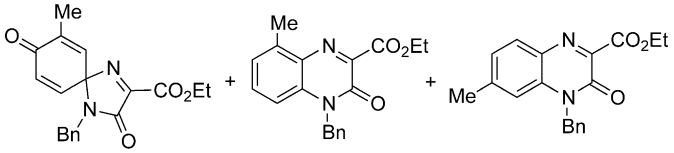
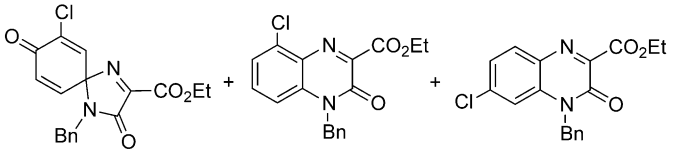
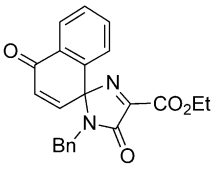
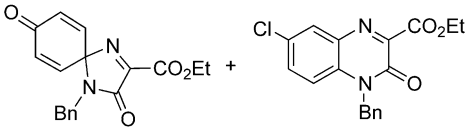
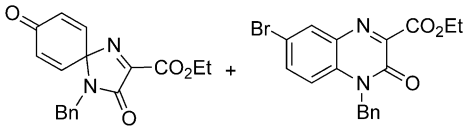
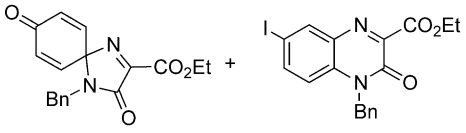
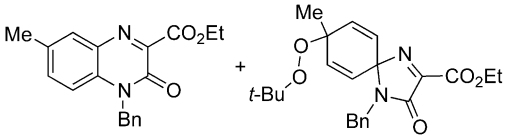
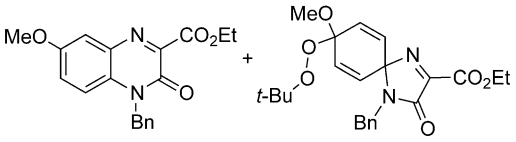
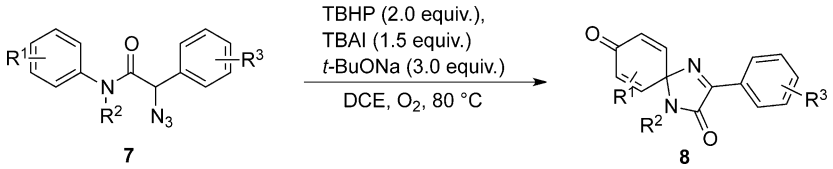
Entry	Substrate	Product (Yield [%]) [b]
1	**1b**, R = *o*-Me	 **2b** (60)
2	**1d**, R = *m*-Me	 **2d** (18) **3d-1** (40) **3d-2** (20)
3	**1f**, R = *m*-Cl	 **2f** (10) **3f-1** (42) **3f-2** (20)
4	**1j**, R = 1,2-naph	 **2j** (50)
5	**1m**, R = *p*-Cl	 **2a** (16) **3m** (45)
6	**1n**, R = *p*-Br	 **2a** (50) **3n** (34)
7	**1o**, R = *p*-I	 **2a** (56) **3o** (28)
8	**1p**, R = *p*-Me	 **3p** (46) **4p'** (36) (*dr*= 3:2) [c]

Table 2. (Continued)

Entry	Substrate	Product (Yield [%]) [b]
9	**1q**, R = *p*-OMe	 **3q** (27) + **4q'** (24) [c]

[a] The reaction was performed on a 0.5 mmol scale in acetonitrile under an argon atmosphere.
[b] Isolated yield.
[c] The relative configuration is undetermined.

Table 3. The reaction of **7** under modified conditions.[a]



7 **8**

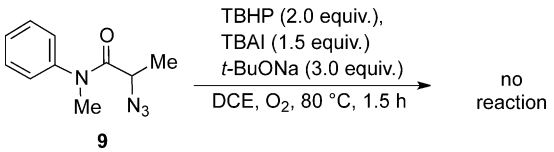
Entry	7	R^1	R^2	R^3	Product/Yield [%][b]
1	**7a**	H	Bn	H	**8a**/99
2	**7b**	*p*-Cl	Bn	H	**8a**/80
3	**7c**	*p*-MeO	Bn	H	**8a**/96
4	**7d**	*o*-Me	Bn	H	**8d**/60
5	**7e**	H	Me	H	**8e**/45
6	**7f**	H	Bn	*m*-Br	**8f**/72
7	**7g**	H	Bn	*p*-Me	**8g**/67
8	**7h**	H	Bn	*p*-Cl	**8h**/93
9	**7i**	H	Bn	*p*-F	**8i**/43
10	**7j**	H	Bn	*o*-Me	**8j**/6[c]

[a] The reaction was performed on a 0.5 mmol scale.
[b] Isolated yield.
[c] With 90% **7j** recovered.

would also be effective for the reaction of compounds **7**. However, our initial experiment showed that no reaction took place when **7** was subjected to the previously mentioned optimal conditions. We assumed that for the reaction of **7** to take place, the α-hydrogen had to be deprotonated first to generate the imine intermediates. Indeed, when 3.0 equiv. of *t*-BuONa were added to the reaction mixture, compounds **7** were converted smoothly to the azaspirocyclohexadienones **8** underan oxygen atmosphere in DCE. The yields were high except for **7e**, **7i** and **7j** (Table 3). The lower yield of **8e** is consistent with the aforementioned observation that the *N*-methyl group is inferior to the *N*-benzyl group to promote the cyclization. These conditions were also applied to compound **9**, but the reaction did not occur (Scheme 12). Probably, the α-H in **9** is not acidic enough for the deprotonation to take place under the indicated conditions.

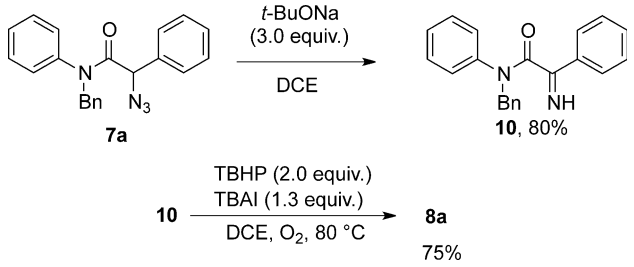
Our control experiment shows that when treated with *t*-BuONa alone, **7a** will extrude a nitrogen molecule almost instantaneously, and after work-up compound **10** can be obtained in roughly 80% yield (Scheme 13). Apparently, the oxidative cyclization of **7** firstly involves the generation of an imine intermediate, which is then oxidized to the corresponding iminyl radical.

It is interesting to see from Table 3 that the *p*-MeO group was as readily removed as the chlorine atom, and **8a** was formed exclusively in both cases. This discrepancy with the reaction outcome of **1q** suggests that the α-phenyl group is detrimental to the forma-

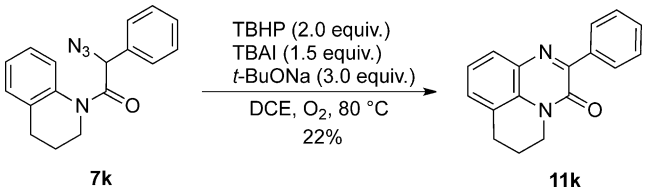


9

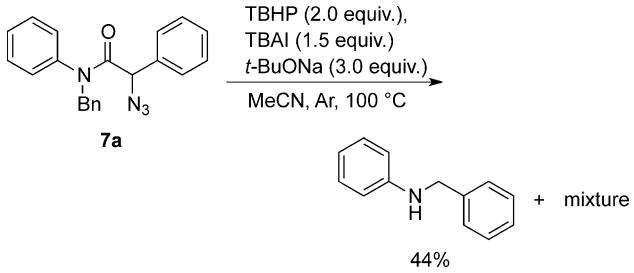
Scheme 12. The result with **9** as the substrate under modified conditions



Scheme 13. Evidence for formation of the iminyl radicals from **7** *via* imine intermediates.



Scheme 14. Reaction of **7k** under an oxygen atmosphere.



Scheme 15. Reaction of **7a** in CH_3CN under an argon atmosphere.

tion of the quinoxalin-2-one ring, and meanwhile the strong basic conditions in the present cases are favorable for the removal of the *p*-MeO group. This hypothesis is supported by the fact that the cyclization of compound **7k** gave quinoxalin-2-one **11k** in only 22% yield (Scheme 14), which is much lower than that of the structurally analogous **1r** under similar conditions (Scheme 9). Moreover, when compound **7a** was subjected to TBHP/TBAI in acetonitrile under an argon atmosphere, no cyclization product was obtained; the reaction only resulted in the decomposition of **7a** (Scheme 15).

Conclusions

In summary, we have demonstrated that the reagent combination of TBHP/TBAI is capable of oxidizing (*N*-aryl-carbamoyl)-2-iminoacetates to the corresponding α-(arylaminocarbonyl)iminyl radicals. With the help of this new method, the cyclization of α-(arylaminocarbonyl)iminyl radicals was investigated with regard to the substituent effect and the influence of oxygen. Our results indicate that the intramolecular *ipso*-attack on the *N*-aryl ring by the iminyl radical is generally more favorable than the *ortho*-attack, and correspondingly in most cases affords azaspirocyclohexadienones as the dominant products under an oxygen atmosphere. By contrast, when the reaction was carried out under an argon atmosphere, the *ortho*-attack products, quinoxalin-2-ones, could be generated as the major product. The substituents have a big influence on the reaction outcome. This oxidizing system is applicable to the reaction of α-phenyl α-azido-*N*-arylamides by adding 3.0 equiv. of *t*-BuONa into the reaction mixture, but in these cases, the formation of the quinoxalin-2-one product becomes very unfavorable. This study not only sheds light on the reactivity of α-(arylaminocarbonyl)iminyl radicals, but also provides a new metal-free protocol for the synthesis of the azaspirocyclohexadienone derivatives.

Experimental Section

Typical Procedure for the Reaction of 1 under an O_2 Atmosphere

To a 25-mL sealed tube equipped with a magnetic stirring bar were added **1a** (168 mg, 0.54 mmol), tetrabutylammonium iodide (TBAI, 240 mg, 1.2 equiv.), *tert*-butyl hydroperoxide (TBHP, ~5.5 M in decane) (185 μL, 1.9 equiv.) and 1,2-dichloroethane (5.0 mL). The solution was stirred in an oil bath at 80 °C under an oxygen atmosphere (with an oxygen balloon). After the reaction was complete as indicated by TLC (1.5 h), the reaction mixture was poured into a saturated aqueous $NaHSO_3$ solution (15 mL), and was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine (30 mL) and dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue was treated by silica gel chromatography to give product **2a**; yield: 149 mg (85%).

General Procedure for the Reaction of 1 under an Argon Atmosphere

To a 25-mL sealed tube equipped with a magnetic stirring bar were added **1** (0.5 mmol, 1.0 equiv.), TBAI (277 mg, 1.5 equiv.), TBHP (70% in water) (140 μL, 2.0 equiv.) and 5.0 mL of acetonitrile (bubbled with argon for 10 min. before use). The solution was stirred in an oil bath at 100 °C under an argon atmosphere. After the reaction was complete as indicated by TLC (generally 2.5–3 h), the reaction mixture was poured into a saturated aqueous $NaHSO_3$ solution (15 mL), and was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine (30 mL) and dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residual was treated byh silica gel chromatography to give the products.

General Procedure for the Reaction of 7 under an O_2 Atmosphere

To a 25-mL sealed tube equipped with a magnetic stirring bar were added **7** (0.5 mmol, 1.0 equiv.), tetrabutylammonium iodide (TBAI, 277 mg, 1.5 equiv.), *tert*-butyl hydroperoxide (TBHP, ~5.5 M in decane) (185 μL, 2.0 equiv.), sodium *tert*-butoxide (*t*-BuONa, 145 mg, 3.0 equiv.) and DCE (5.0 mL). The solution was stirred in an oil bath at 80 °C under an oxygen atmosphere. After the reaction was complete as indicated by TLC (generally 1–1.5 h), the reaction mixture was poured into a saturated aqueous $NaHSO_3$ solution (15 mL), and was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine (30 mL) and dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residual was treated by silica gel chromatography to give products **8**.

Caution: *tert*-butyl hydroperoxide is hazardous and flammable. When used in the presence of oxygen it should be handled with care and proper protections.

Acknowledgements

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

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the absorption of the N_3 group, whereas in the FT-IR spectra of **1**, this peak is absent. In the latter cases, an absorption corresponding to an N−H stretch vibration appears at about 3200 cm^{-1}. We apologize for these terrible mistakes in the previous paper caused by our negligence.

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