有机化学 DOI: 10.6023/cjoc202110022 研究论文
Chinese Journal of Organic Chemistry ARTICLE

紫外光引发胺基苯酚与胺的自由基偶联反应构筑二胺基苯醌亚胺类化合物

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摘要 报道了一种在无金属条件下, 使用廉价易得的叔丁基过氧化氢为氧化剂, 紫外光照射引发胺基苯酚与胺类化合物发生自由基偶联反应, 高效地构筑二胺基苯醌亚胺类化合物. 该反应能够为合成具有潜在药物活性的醌亚胺分子提供这一种操作简单、环境友好且避免使用金属催化剂或光催化剂的新途径.

关键词 紫外光; 自由基偶联; 无金属; 二胺基苯醌亚胺

Construction of Diaminobenzoquinone Imines through Radical Coupling of Aminophenols with Amine under UV-Light

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Abstract A metal-free radical coupling reaction of aminophenols with amines under UV-light has been successfully developed to synthesize diaminobenzoquinone imines in high yields, in which the commercially available and cheap *t*-butyl hydroperoxide (TBHP) was used as an oxidant. This protocol provides an easy and green approach for the construction of benzoquinone imines with potential pharmaceutical interest avoiding metal catalyst or photocatalyst.

Keywords UV-light; radical coupling; metal-free; diaminobenzoquinone imines

1 Introduction

Quinone framework is ubiquitous in pharmaceutical and material sciences.[1] Among them, benzoquinone imines are important synthons in organic synthesis, which are also widely used in the dye industry and inhibitors against the photo-oxidation of polymers.[2] As a result, the establishment of robust synthetic approaches for their preparation starting from readily available materials has been continuously needed. For example, Rajappa group[3] reported an intramolecular regioselective addition of benzoquinone imines for the synthesis of 5-acylaminobenzimi-dazole-2-carbamates in 1983. In 2001, Nair group[4] reported a facile route to bicyclo[3.2.1] and bicyclo[2.2.1] systems through dipolar cycloaddition of carbonyl ylides with *para*-benzoquinone imines. In addition, they[5] also reported a facile synthesis of spiro-fused *γ*-iminolactams using three component reaction involving isocyanides, dimethyl acetylenedicarboxylate and benzoquinone imines. In 2016, Parker group[6] synthesized dihydroquinolines, quinolines and indoles through heterocycle annulation of enolizable vinyl benzoquinone imines. Recently, photocatalysis have attracted more and more attention in the organic synthesis due to its ability to promote bond formation under green and mild reaction conditions.[7] Especially, N-centered radicals enabled by photocatalysis have been recognized as potent synthetic intermediates.[8] As well-known, the UV-initiated radical polymerization with photoinitiators, such as benzo-

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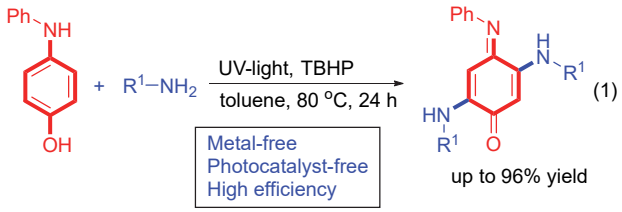
Received October 15, 2021; revised November 17, 2021; published online December 2, 2021.

Project supported by the Fujian Education and Scientific Research Project for Young and Middle-Aged Teachers (No. JAT190990).

福建省中青年教师教育科研(No. JAT190990)资助项目.

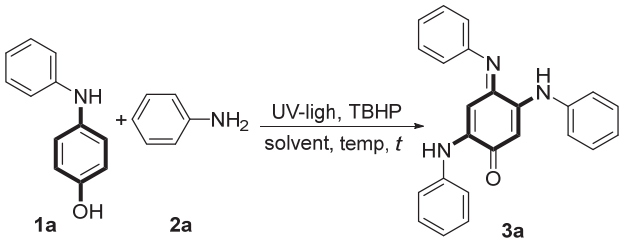
phenones, has been demonstrated to exhibit fast rate, high yield and room operation characters due to the high initiator decomposition rate and the low activation energy.[9] Recently, our group[10] has developed a ferrocene-initiated radical reaction of benzoquinone with amines for the direct access to diaminobenzoquinone imines in high yields, however, the products were limited to the same substituent groups at three N atoms. For this direction, in our continuing effort to develop more efficient method in the synthesis of diaminobenzoquinone imines, herein, we present a metal-free radical coupling reaction of aminophenols with amines under UV-light to synthesize diaminobenzoquinone imines (Eq. 1), in which various substituents at N atoms could be tolerated. This protocol provides an easy and green approach for the construction of benzoquinone imines with potentially pharmaceutical interest avoiding metal catalyst or photocatalyst.



2 Results and discussion

At the outset of our studies, 4-(phenylamino)phenol (**1a**) and aniline (**2a**) were chosen as the model substrates to optimize the reaction conditions (Table 1). To our great delight, (*E*)-2,5-bis(phenylamino)-4-(phenylimino)cyclohexa-2,5-dienone (**3a**) was obtained as a main product in 85% yield in toluene at 80 ℃ under UV-light (λ_{max}=365 nm, 250 W) in air, in which *t*-BuOOH (TBHP, 3.0 equiv.) was used as an oxidant (Table 1, Entry 1). Only 35% yield of **3a** was obtained when the reaction was carried out without UV-light (Table 1, Entry 1 vs. Entry 2). When the reaction was carried out under N_2 and O_2, the target product **3a** was obtained in 82% and 85% yields, which indicated that the atmosphere had no significant effect on the reaction (Table 1, Entries 2, 3). The yield of target product (**3a**) was decreased to 71% and 62%, when the power of UV was reduced to 200 and 150 W (Table 1, Entries 4, 5). Moreover, 4.0 equiv. of TBHP favored this reaction, and the yield of **3a** could be increased to 96% yield (Table 1, Entries 7～12). Toluene was proved to be better than other solvents, including dimethyl sulfoxide (DMSO), *N*,*N*-dime- thylformamide (DMF), *N*-methyl pyrrolidone (NMP), dioxane, CH_3OH and CH_3CN (Table 1, Entry 10 vs. Entries 13～18). In addition, the yield of **3a** was decreased when the reaction temperature and reaction time were either increased or decreased (Table 1, Entries 19～22). Based on the results, the optimal reaction conditions were identified as follows: toluene as solvent, at 80 ℃, and ^{t}BuOOH (TBHP) (4.0 equiv.) as an oxidant under UV-light (λ_{max}=365 nm, 250 W) in air for 24 h (Table 1, Entry 10).

Table 1 Optimization of reaction conditions[a]

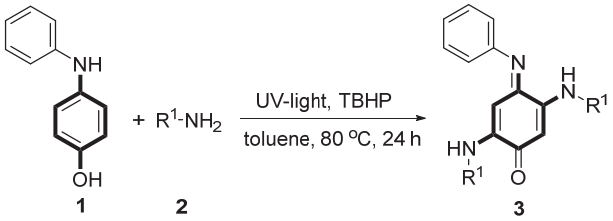


Entry	UV-light (λ_{max}, *P*)	TBHP/ equiv.	Solvent	*T*/℃	Yiled[b]/%
1	365 nm, 250 W	3.0	Toluene	80	85
2	—	3.0	Toluene	80	35
3[c]	365 nm, 250 W	3.0	Toluene	80	82
4[d]	365 nm, 250 W	3.0	Toluene	80	85
5	365 nm, 200 W	3.0	Toluene	80	71
6	365 nm, 150 W	3.0	Toluene	80	62
7	365 nm, 250 W	—	Toluene	80	21
8	365 nm, 250 W	2.0	Toluene	80	51
9	365 nm, 250 W	1.0	Toluene	80	30
10	**365 nm, 250 W**	**4.0**	**Toluene**	**80**	**96**
11	365 nm, 250 W	5.0	Toluene	80	96
12	365 nm, 250 W	6.0	Toluene	80	92
13	365 nm, 250 W	4.0	DMSO	80	Trace
14	365 nm, 250 W	4.0	DMF	80	33
15	365 nm, 250 W	4.0	NMP	80	65
16	365 nm, 250 W	4.0	Dioxane	80	61
17	365 nm, 250 W	4.0	CH_3OH	80	Trace
18	365 nm, 250 W	4.0	CH_3CN	80	27
19	365 nm, 250 W	4.0	Toluene	90	89
20	365 nm, 250 W	4.0	Toluene	70	86
21[e]	365 nm, 250 W	4.0	Toluene	80	95
22[f]	365 nm, 250 W	4.0	Toluene	80	87

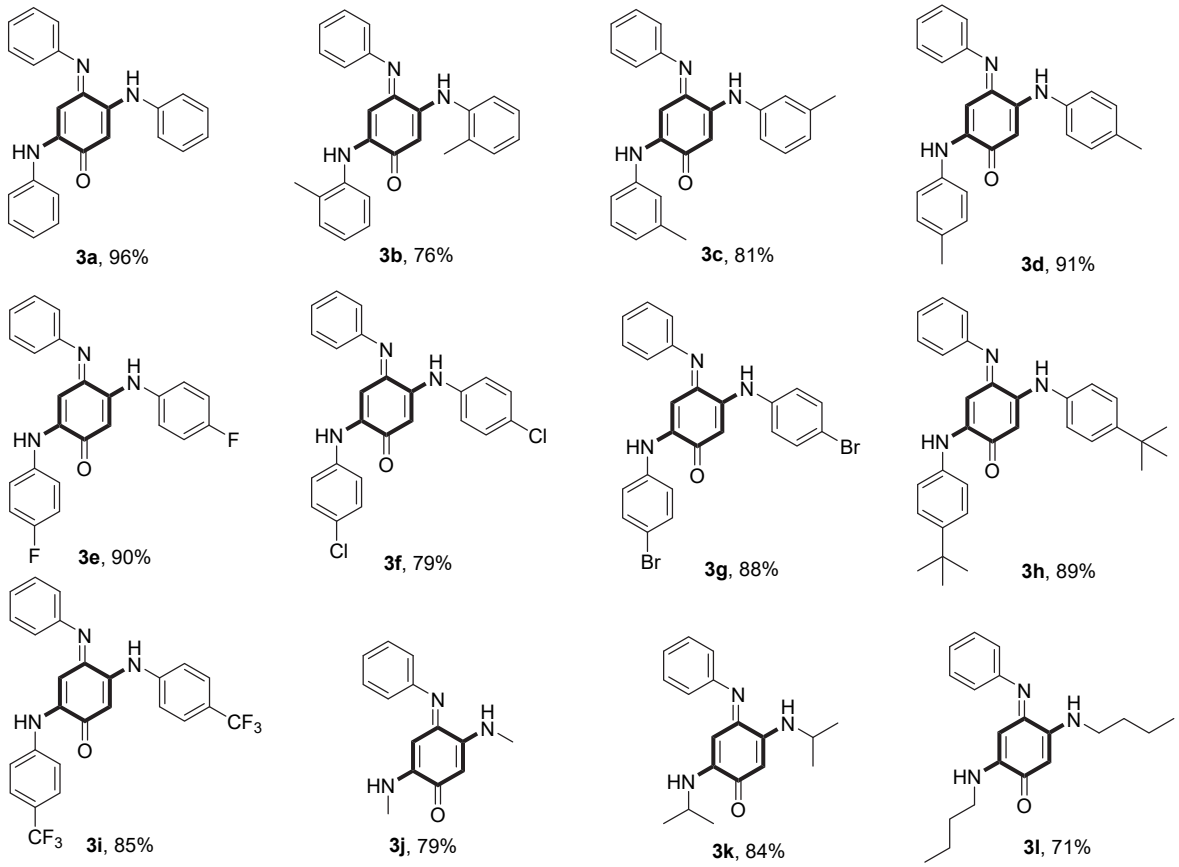
[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.6 mmol), TBHP (70% solution in ethyl acetate), solvent (2.0 mL), 24 h. [b] Isolated yields. [c] N_2. [d] O_2. [e] 26 h. [f] 22 h.

With the optimized reaction conditions in hand, the scope of the substrates was examined (Table 2). 4-(Phenylamino)-phenol (**1a**) reacted smoothly with various amines (**2a**～**2l**) to give the desired products (**3a**～**3l**) in moderate to good yields (71%～96%). Methyl group at the *ortho*-, *meta*-, and *para*-position of aniline provided the corresponding products **3b**～**3d** in 76%, 81% and 91% yields, which indicated that steric effect of substituted groups did not obviously impact on this transformation. Halogen groups, such as F, Cl, and Br at the 4-position of aniline provided the corresponding products **3e**～**3g** in 90%, 79%, and 88% yields, respectively. Other groups, such as *t*-butyl and trifluoromethyl, could be well tolerated and gave the corresponding products in satisfactory yields (**3h** and **3i**) (89% and 85%), which indicated that the electron density on the moiety of the aniline did also not significantly affect the efficiency of the coupling reaction. Moreover, methylamine, isopropylamine, and *n*-butylamine could also reacted with **1a** to provide the corresponding products **3j**～**3l** in 79%, 84%,

Table 2 Scope of substrates[a,b]



1 2 3



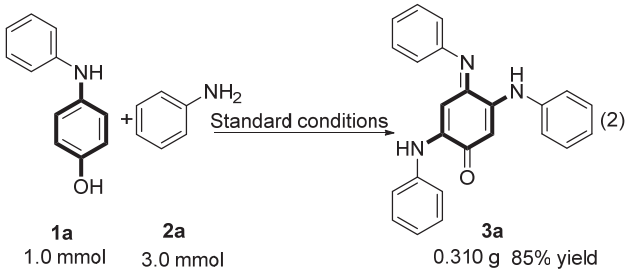
[a] Reaction conditions: **1** (0.20 mmol), **2** (0.6 mmol), TBHP (4.0 equiv.), solvent (2.0 mL). [b] Isolated yields.

and 71% yields, respectively. However, other aminophenol or secondary amine, such as 4-aminophenol or *N*-methylaniline, failed to give the desired products.

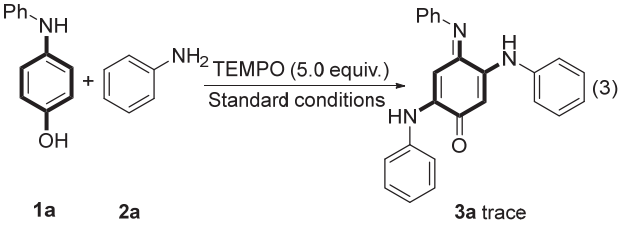
To prove the practicality of this ingenious reaction system, a 1 mmol-scale synthesis of the **3a** was performed. When 1.0 mmol (0.185 g) of 4-(phenylamino)phenol (**1a**) and 3.0 mmol (0.279 g) of aniline (**2a**) were loaded, the corresponding product (**3a**) was obtained in 85% yield (0.310 g) (Eq. 2). Therefore, this reaction could possess extensive applications in organic synthesis and pharmaceutical industry.

To clarify the reaction mechanism, control experiment was carried out (Eq. 3). When TEMPO (5.0 equiv.), a radical scavenger, was introduced into the reaction under standard conditions, only trace target product (**3a**) was detected by GC, which suggested that a radical pathway was involved in this reaction.

Based on the references and our previous work,[11] a

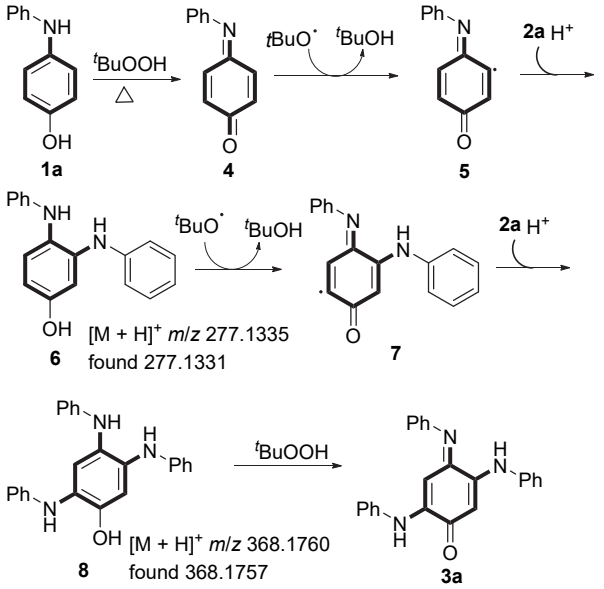


1a 1.0 mmol **2a** 3.0 mmol **3a** 0.310 g 85% yield



1a **2a** **3a** trace

plausible reaction mechanism was proposed as shown in Scheme 1. First, 4-(phenylamino)phenol (**1a**) could be easily oxidized to 4-(phenylimino)cyclohexa-2,5-dienone (**4**) by TBHP under heat. Then, the *tert*-butoxyl radical generated from TBHP abstracts the H-atom of 4-(phenylimino)-cyclohexa-2,5-dienone (**4**) to give a radical intermediate **5**, which could react with **2a** to generate intermediate **6** (detected by HRMS). Subsequently, radical intermediate **7** was formed from the reaction of *tert*-butoxyl radical with compound **6**, which could react with **2a** to give 2,4,5-tris(phenylamino)phenol (**8**) (detected by HRMS). Finally, the intermediate **8** could be oxidized by TBHP to the target product **3a**.



Scheme 1 Proposed reaction mechanism

3 Conclusions

In summary, we have demonstrated a metal-free coupling reaction of aminophenols with amines under UV-light for the direct access to diaminobenzoquinone imines in high yields, in which the commercially available and cheap TBHP was used as an oxidant. This protocol provides an easy and green approach for the construction of benzoquinone imines with potential pharmaceutical interest and avoiding metal catalyst or photocatalyst. Further study on the application of this radical reaction system is ongoing in our laboratory.

4 Experimental section

4.1 General experimental information

All manipulations were conducted in a standard Schlenk technique under air atmosphere. Unless otherwise stated, all commercial materials and solvents were used directly without further purification. Commercially available chemicals were obtained from Energy Chemical, TCI, Alfa Aesar, J&K. ^{1}H NMR and ^{13}C NMR spectra were measured on a 400 MHz Bruker spectrometer (^{1}H NMR 400 MHz, ^{13}C NMR 100 MHz), using DMSO-d_6 as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are reported from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ_H 7.26, δ_C 77.2; DMSO-d_6: δ_H 2.50, δ_C 39.5). Column chromatography was performed on silica gel (70～230 mesh ASTM) using the reported eluents. Thin-layer chromatography (TLC) was carried out on 15 cm×4 plates with a layer thickness of 0.2 mm (silica gel 60 F254).

4.2 Experimental method

To a 20 mL flame-dried Schlenk tube were added **1** (0.20 mmol), **2** (0.60 mmol) and TBHP (0.80 mmol), and followed by addition of toluene (2.0 mL). The formed mixture was stirred in 80 ℃ oil bath under UV-light (λ_{max}=365 nm, 250 W) in air for 24 h. The reaction was monitored by TLC. The solution was then quenched with H_2O (10.0 mL), extracted with ethyl acetate (10.0 mL×3). The combined organic phases were washed with saturated sodium bicarbonate solution, dried over sodium sulfate, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate, V∶V=20∶1 to 4∶1) to afford the desired products **3**.

4.3 Procedure for the synthesis of product **3a** on a 1.0 mmol scale

To a flame-dried Schlenk tube were added **1a** (185.0 mg, 1.0 mmol), **2a** (279.0 mg, 3.0 mmol) and TBHP (360.0 mg, 4.0 mmol), followed by addition of toluene (10.0 mL). The formed mixture was stirred in 80 ℃ oil bath under UV-light (λ_{max}=365 nm, 250 W) in air for 24 h. The reaction was monitored by TLC. The solution was then quenched with H_2O (60.0 mL), extracted with ethyl acetate (20.0 mL×3). The combined organic phases were washed with saturated sodium bicarbonate solution, dried over sodium sulfate, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate, V∶V=20∶1) to afford the desired products **3a** (310.0 mg, 85% yield).

4.4 Characterization of the product

(*E*)-2,5-Bis(phenylamino)-4-(phenylimino)cyclohexa-2,5-dienone (**3a**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Yield 96% (70 mg). Brown solid: m.p. 204～205 ℃. (lit. 203～204 ℃)[10]. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.28 (s, 1H), 8.61 (s, 1H), 7.48～7.37 (m, 6H), 7.23 (dt, J=23.4, 7.9 Hz, 5H), 7.12 (t, J=7.4 Hz, 1H), 7.01 (dd, J=16.6, 7.4 Hz, 3H), 5.96 (s, 1H), 5.87 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 180.0, 153.8, 149.8, 149.6, 141.2, 138.8, 138.3, 129.3, 128.9, 128.8, 125.2, 124.2, 123.9, 123.9, 122.0, 120.8, 96.6, 90.1; HRMS (ESI) calcd for $C_{24}H_{20}N_3O$ $[M+H]^+$ 366.1601, found 366.1602.

(*E*)-4-(Phenylimino)-2,5-bis(*o*-tolylamino)cyclohexa-2,5-dienone (**3b**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Yield 76% (60 mg). Brown liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.10 (s, 1H), 8.19 (s, 1H),

7.39～7.24 (m, 6H), 7.19 (d, J=7.3 Hz, 1H), 7.07～7.12 (m, 4H), 6.89 (d, J=7.5 Hz, 2H), 5.34 (s, 1H), 5.20 (s, 1H), 2.25 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 179.5, 153.5, 151.7, 149.6, 142.9, 136.7, 136.6, 134.2, 133.1, 131.0, 130.8, 129.3, 128.7, 126.8, 126.8, 126.3, 125.7, 124.9, 124.0, 120.7, 95.7, 88.6, 17.5, 17.4; HRMS (ESI) calcd for $C_{26}H_{24}N_3O$ $[M+H]^+$ 394.1914, found 394.1909.

(*E*)-4-(Phenylimino)-2,5-bis(*m*-tolylamino)cyclohexa-2,5-dienone (**3c**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Yield 81% (64 mg). Brown liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.19 (s, 1H), 8.53 (d, J=8.5 Hz, 1H), 7.48～7.25 (m, 3H), 7.21 (d, J=10.8 Hz, 2H), 7.17～6.93 (m, 6H), 6.88～6.75 (m, 2H), 5.98 (d, J=1.5 Hz, 1H), 5.87 (s, 1H), 2.35 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 180.1, 153.9, 149.7, 141.1, 138.7, 138.2, 129.1, 128.8, 128.6, 125.9, 124.7, 124.4, 124.2, 124.2, 122.1, 121.3, 120.9, 120.8, 119.3, 117.9, 96.7, 90.3, 21.0, 21.0; HRMS (ESI) calcd for $C_{26}H_{24}N_3O$ $[M+H]^+$ 394.1914, found 394.1914.

(*E*)-4-(Phenylimino)-2,5-bis(*p*-tolylamino)cyclohexa-2,5-dienone (**3d**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Brown solid. Yield 91% (72 mg), m.p. 198～199 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.62 (d, J=8.3 Hz, 1H), 7.60 (d, J=3.4 Hz, 1H), 7.37 (t, J=7.9 Hz, 1H), 7.23～7.01 (m, 8H), 6.95 (t, J=8.4 Hz, 3H), 6.87 (d, J=8.2 Hz, 1H), 6.12 (dd, J=25.1, 17.4 Hz, 2H), 2.36 (s, 3H), 2.28 (d, J=5.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 181.0, 153.5, 150.1, 146.73 (s), 140.8, 136.2, 135.2, 134.3, 133.6, 129.9, 129.5, 128.9, 124.5, 123.1, 121.1, 120.8, 96.7, 90.1, 21.0, 20.8; HRMS (ESI) calcd for $C_{26}H_{24}N_3ONa$ $[M+Na]^+$ 416.1733, found 416.1729.

(*E*)-2,5-Bis((4-fluorophenyl)amino)-4-(phenylimino)-cyclohexa-2,5-dienone (**3e**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). White solid. Yield 90% (72 mg), m.p. 205～206 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.23 (s, 1H), 8.58 (s, 1H), 7.37 (ddd, J=20.7, 11.3, 6.4 Hz, 4H), 7.24 (t, J=8.8 Hz, 2H), 7.19～7.03 (m, 5H), 6.92 (d, J=7.4 Hz, 2H), 5.78 (s, 1H), 5.68 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 180.0, 160.6, 159.7, 158.2, 157.3, 153.7, 150.4, 149.5, 141.7, 135.2, 128.9, 126.4 (d, J=8.5 Hz), 124.4 (d, J=8.2 Hz), 120.8, 116.0 (d, J=22.7 Hz), 115.7 (d, J = 22.6 Hz), 96.4, 89.6; ^{19}F NMR (376 MHz, DMSO-d_6) δ: −116.7, −118.1; HRMS (ESI) calcd for $C_{24}H_{18}F_2N_3O$ $[M+H]^+$ 402.1412, found 402.1413.

(*E*)-2,5-Bis((4-chlorophenyl)amino)-4-(phenylimino)-cyclohexa-2,5-dienone (**3f**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Brown solid. Yield 79% (69 mg), m.p. 247～248 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.29 (s, 1H), 8.69 (s, 1H), 7.49～7.34 (m, 6H), 7.31～7.23 (m, 2H), 7.19 (t, J=9.9 Hz, 2H), 7.11 (t, J=7.4 Hz, 1H), 6.97 (dd, J=17.8, 8.0 Hz, 2H), 5.89 (d, J=15.2 Hz, 1H), 5.84 (d, J=3.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 180.2, 153.6, 149.4, 140.9, 137.9, 137.3, 129.2, 128.9, 128.8, 127.4, 125.5, 124.4, 123.7, 123.5, 122.7, 120.8, 97.2, 90.8; HRMS (ESI) calcd for $C_{24}H_{18}Cl_2N_3O$ $[M+H]^+$ 434.0821, found 434.0818.

(*E*)-2,5-Bis((4-bromophenyl)amino)-4-(phenylimino)-cyclohexa-2,5-dienone (**3g**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Brown liquid. Yield 88% (92 mg). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.32 (s, 1H), 8.72 (s, 1H), 7.62 (d, J=8.6 Hz, 3H), 7.42 (dd, J=15.0, 8.3 Hz, 5H), 7.16 (d, J=8.4 Hz, 3H), 6.99 (d, J=7.8 Hz, 2H), 5.91 (dd, J=14.8, 11.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 180.7, 154.0, 149.8, 141.3, 138.8, 138.2, 132.6, 132.2, 129.4, 126.3, 125.0, 124.4, 122.7, 121.3, 117.6, 116.0, 97.8, 91.4; HRMS (ESI) calcd for $C_{24}H_{18}Br_2N_3O$ $[M+H]^+$ 521.9811, found 521.9809.

(*E*)-2,5-Bis((4-(*tert*-butyl)phenyl)amino)-4-(phenylimino)cyclohexa-2,5-dienone (**3h**): Eluent: petroleum ether/ethyl acetate (V∶V=10∶1). Brown liquid. Yield 89% (76 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.62 (s, 1H), 7.62～7.55 (m, 1H), 7.44～7.34 (m, 5H), 7.27～7.10 (m, 4H), 7.02～6.87 (m, 4H), 6.16 (d, J=3.4 Hz, 1H), 6.11 (d, J=3.3 Hz, 1H), 1.34 (s, 9H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 181.3, 157.7, 154.2, 150.1, 148.7, 147.8, 147.2, 140.9, 136.3, 135.5, 129.1, 126.3, 125.9, 123.0, 120.9, 119.8, 97.0, 90.8, 34.7, 34.5, 31.6, 31.4; HRMS (ESI) calcd for $C_{32}H_{36}N_3O$ $[M+H]^+$ 478.2853, found 489.2853.

(*E*)-4-(Phenylimino)-2,5-bis((4-(trifluoromethyl)phenyl)amino)cyclohexa-2,5-dienone (**3i**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Brown liquid. Yield 85% (85 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.75 (s, 1H), 7.75 (s, 1H), 7.68 (d, J=8.5 Hz, 2H), 7.51 (d, J=8.5 Hz, 2H), 7.44 (t, J=7.8 Hz, 4H), 7.22 (t, J=7.5 Hz, 1H), 7.11 (d, J=8.5 Hz, 2H), 6.99～6.93 (m, 2H), 6.31 (d, J=8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 181.2, 153.6, 149.0, 148.3, 142.0, 141.5, 139.6, 129.6, 129.4, 129.2, 127.1 (dd, J=7.7, 3.9 Hz), 126.9 (dd, J=7.6, 3.9 Hz), 125.6, 122.3, 122.2 121.1 (d, J=4.5 Hz), 120.9, 119.9, 98.8, 92.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −62.1, −62.3; HRMS (ESI) calcd for $C_{26}H_{18}F_6N_3O$ $[M+H]^+$ 502.1349, found 502.1344.

(*E*)-2,5-Bis(methylamino)-4-(phenylimino)cyclohexa-2,5-dienone (**3j**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Brown liquid. Yield 79% (38 mg). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.70 (d, J=5.2 Hz, 1H), 7.30 (t, J=7.7 Hz, 2H), 7.02 (t, J=7.4 Hz, 1H), 6.86 (d, J=5.2 Hz, 1H), 6.79 (d, J=7.8 Hz, 2H), 5.15 (s, 1H), 4.87 (s, 1H), 2.73 (d, J=5.2 Hz, 3H), 2.41 (d, J=5.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 178.2, 154.4, 153.5, 150.5, 146.8, 129.0, 123.4, 120.4, 93.2, 84.9, 29.0, 28.4; HRMS (ESI) calcd for $C_{14}H_{16}N_3O$ $[M+H]^+$ 242.1288, found 242.1293.

(*E*)-2,5-Bis(isopropylamino)-4-(phenylimino)cyclohexa-2,5-dienone (**3k**): Eluent: petroleum ether/ethyl acetate (V∶V=20∶1). Brown liquid. Yield 84% (50 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36 (t, J=7.7 Hz, 2H), 7.10 (t, J=7.4 Hz, 1H), 6.92 (dd, J=20.7, 7.3 Hz, 3H), 5.78 (d, J=7.5 Hz, 1H), 5.41 (s, 1H), 5.13 (s, 1H), 3.65 (dt, J=13.2, 6.5 Hz, 1H), 3.29 (dt, J=13.1, 6.5 Hz, 1H), 1.29 (d, J=6.5 Hz, 6H), 1.11 (d, J=6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.9, 153.8, 152.7, 150.5, 144.5, 129.1, 123.9, 121.0, 94.4, 86.7, 44.2, 43.4, 22.1, 22.0; HRMS (ESI) calcd for $C_{18}H_{24}N_3ONa$ $[M+Na]^+$ 320.1733, found 320.1734.

(*E*)-2,5-Bis(butylamino)-4-(phenylimino)cyclohexa-2,5-dienone (**3l**): Eluent: petroleum ether/ethyl acetate (*V*∶*V*=20∶1). Brown liquid. Yield 71% (46 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36 (t, *J*=7.8 Hz, 2H), 7.09 (dd, *J*=21.2, 13.8 Hz, 2H), 6.89 (d, *J*=7.4 Hz, 2H), 5.85 (s, 1H), 5.40 (s, 1H), 5.14 (s, 1H), 3.18 (dd, *J*=13.1, 6.9 Hz, 2H), 2.88 (dd, *J*=12.8, 6.8 Hz, 2H), 1.67 (dd, *J*=14.9, 7.6 Hz, 2H), 1.51 (dd, *J*=14.7, 7.2 Hz, 2H), 1.44 (dd, *J*=15.1, 7.4 Hz, 2H), 1.32 (dd, *J*=15.2, 7.2 Hz, 2H), 0.97 (t, *J*=7.3 Hz, 3H), 0.87 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.8, 153.9, 153.8, 150.5, 145.8, 129.1, 123.9, 121.0, 94.1, 86.3, 42.6, 42.0, 30.6, 30.6, 20.5, 20.3, 13.9, 13.9; HRMS (ESI) calcd for $C_{20}H_{28}N_3O$ $[M+H]^+$ 326.2227, found 326.2224.

Supporting Information ^{1}H NMR and ^{13}C NMR spectra of compounds **3a** ~ **3l**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

References

[1] (a) Fabre, B. *Chem. Rev.* **2016**, *116*, 4808.
(b) Cavalli, A.; Bolognesi, M. L.; Capsoni, S.; Andrisano, V.; Bartolini, M.; Margotti, E.; Cattaneo, A.; Recanatini, M.; Melchiorre, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 3689.
(c) Nachtsheim, B. J. *Nat. Chem.* **2020**, *12*, 326.
(d) Liu, S.; Shen, T.; Luo, Z.; Liu, Z. *Chem. Commun.* **2019**, *55*, 402.

[2] (a) Yu, J.; Zhang, H.; Lu, Q.; Ding, X.; Liu, S.; Li, Y. *Chem. Ind. Eng. Prog.* **2015**, *34*, 1115.
(b) Halhalli, M. R.; Sellergren, B. *Polym. Chem*. **2015**, *6*, 7320.

[3] Rajappa, S.; Sreenivasan, R.; Rane, A. V. *Tetrahedron Lett*. **1983**, *24*, 3155.

[4] Nair, V.; Rajesh, C.; Dhanya, R.; Vinod, A. U. *Tetrahedron Lett*. **2001**, *42*, 2045.

[5] Nair, V.; Dhanya, R.; Viji, S. *Tetrahedron* **2005**, *61*, 5843.

[6] Parker, K. A.; Mindt, T. L. *Org. Lett*. **2016**, *4*, 4265.

[7] (a) Romero, N. A.; Nicewicz, D. A. *Chem. Rev*. **2016**, *116*, 10075.
(b) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev*. **2013**, *113*, 5322.
(c) Ravelli, D.; Fagnoni, M.; Albini, A. *Chem. Soc. Rev*. **2013**, *42*, 97.
(d) Tobisu, M.; Furukawa, T.; Chatani, N. *Chem. Lett*. **2013**, *42*, 1203.
(e) Gomes, F.; Narbonne, V.; Blanchard, F.; Maestri, G.; Malacria, M. *Org. Chem. Front.* **2015**, *2*, 464.
(f) Wu, Y.; Pi, C.; Cui, X.; Wu, Y. *Org. Lett*. **2020**, *22*, 361.
(g) Ren, J.; Yan, X.; Cui, X.; Pi, C.; Wu, Y.; Cui, X. *Green Chem*. **2020**, *22*, 265.
(h) Huang, Y.; Pi, C.; Tang, Z.; Wu, Y.; Cui, X. *Chin. Chem. Lett*. **2020**, *31*,3237.
(i) Yao, Z.; Lin, X.; Chauvin, R.; Wang, L.; Gras, E.; Cui, X. *Chin. Chem. Lett*. **2020**, *31*, 3250.
(j) Wang, Y.; Gao, X.; Ji, J.; Cui, X.; Pi, C.; Zhao, L.; Wu, Y. *Chin. Chem. Lett*. **2021**, *32*, 1696.
(k) Li, H.; Han, Y.; Yang, Z.; Yao, Z.; Wang, L.; Cui, X. *Chin. Chem. Lett*. **2021**, *32*, 1709.
(l) Ren, J.; Huang, Y.; Pi, C.; Cui, X.; Wu, Y. *Chin. Chem. Lett*. **2021**, *32*, 2592.
(m) Chen, Z.; Zhang, H.; Zhou, S.; Cui, X. *Chin. J. Org. Chem*. **2020**, *40*, 3866 (in Chinese).
(陈志超, 张红, 周树峰, 崔秀灵, 有机化学, **2020**, *40*, 3866.)
(n) Xiao, Y.; Yang, Y.; Zhang, F.; Feng, Y.; Cui, X. *Chin. J. Org. Chem*. **2021**, *41*, 4808 (in Chinese).
(肖玉娟, 杨阳, 张凡, 冯亚栋, 崔秀灵, 有机化学, **2021**, *41*, 4808.)
(o) Wu, Y.; Chen, J.; Ning, J.; Jiang, X.; Deng, J.; Deng, Y.; Xu, R.; He, W. *Green Chem*. **2021**, *23*, 3950.
(p) Yi, R.; He, W. *Chin. J. Org. Chem*. **2021**, *41*, 1267 (in Chinese).
(易荣楠, 何卫民, 有机化学, **2021**, *41*, 1267).

[8] Kwon, K.; Simons, R. T.; Nandakumar, M.; Roizen, J. L. *Chem. Rev.* **2022**, *122*, 2353.

[9] Vitale, A.; Bongiovanni, R.; Ameduri, B. *Chem. Rev.* **2015**, *115*, 8835.

[10] Feng, Y.; Liu, Y.; Fu, Q.; Zou, Z.; Shen, J.; Cui, X. *Chin. Chem. Lett*. **2020**, *31*, 733.

[11] (a) Liang, D.; Tan, L.; Xiao, W.; Chen, J. *Chem. Commun*. **2020**, *56*, 3777.
(b) Xie, L.; Fang, T.; Tan, J.; Zhang, B.; Cao, Z.; Yang, L.; He, W. *Green Chem*. **2019**, *21*, 3858.
(c) Zhu, S.; Zhou, J.; Wu, Q.; Hao, W.; Tu, S.; Jiang, B. *Org. Chem. Front*. **2020**, *7*, 2975.
(d) Feng, Y.; Wu, Z.; Chen, T.; Fu, Q.; You, Q, Shen, J.; Cui, X. *Chin. Chem. Lett*. **2020**, *31*, 3263.
(e) Yu, X.; Chen, J.; Chen, H.; Xiao, W.; Chen, J. *Org. Lett*. **2020**, *22*. 2333.
(f) Zhao, Q.; Zhou, X.; Xu, S.; Wu, Y.; Xiao, W.; Chen, J. *Org. Lett*. **2020**, *22*, 2470.
(g) Shen, Z.; Pi, C.; Cui, X.; Wu, Y. *Chin. Chem. Lett*. **2019**, *30*, 1374.
(h) Gao, Q.; Hao, W.; Liu, F.; Tu, S.; Wang, S.; Li, G.; Jiang, B. *Chem. Commun*. **2016**, *52*, 900.
(i) Zhou, P.; Wang, J.; Zhang, T. *Chem. Commun*. **2018**, *54*, 164.
(j) Yu, H.; Pi, C.; Wang, Y.; Cui, X.; Wu, Y. *Chin. J. Org. Chem*. **2018**, *38*, 124 (in Chinese).
(余海洋, 皮超, 王勇, 崔秀灵, 吴养洁, 有机化学, **2018**, *38*, 124.)
(k) Shi, Z.-J.; Wang, L.-H.; Cui, X. *Chin. J. Org. Chem*. **2019**, *39*, 1596 (in Chinese).
(施兆江, 王连会, 崔秀灵, 有机化学, **2019**, *39*, 1596.)
(l) Liu, R.; Yang, M.; Qiu, G.; Zhang, L.; Wang, Y.; Luo, J. *Chin. J. Org. Chem*. **2020**, *40*, 2071 (in Chinese).
(刘仁志, 杨民, 邱观音生, 张莲鹏, 王玉超, 罗劲, 有机化学, **2020**, *40*, 2071.)
(m) Peng, S.; Lin, Y.; He, W. *Chin. J. Org. Chem*. **2020**, *40*, 541 (in Chinese).
(彭莎, 林英武, 何卫民, 有机化学, **2020**, *40*, 541.)
(n) Yuan, X.; Yang, G.; Yu, B. *Chin. J. Org. Chem*. **2020**, *40*, 3620 (in Chinese).
(袁晓亚, 杨国平, 於兵, 有机化学, **2020**, *40*, 3620.)

(Lu, Y.)

