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Coupling of *N*-Nosylhydrazones with Nitrosoarenes: Transition-Metal-Free Approach to (*Z*)-*N*-Arylnitrones

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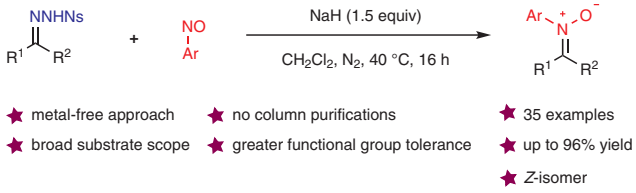

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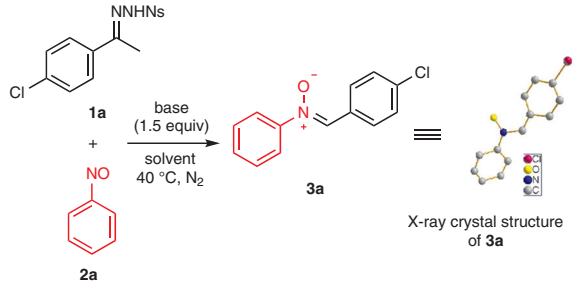
Abstract An efficient and transition-metal-free protocol for the synthesis of (*Z*)-*N*-arylnitrones from the direct coupling of *N*-nosylhydrazones with nitrosoarenes under mild conditions is described. The protocol is compatible with a wide range of functional groups placed on both the reagents and provided the corresponding nitrones in good to excellent yields by simple recrystallization process. The use of these 1,3-dipoles for the synthesis of substituted indoles is elaborated for 2,3-diphenyl-1*H*-indole.

Key words synthetic methods, *N*-nosylhydrazones, (*Z*)-*N*-arylnitrones, nitrosoarenes, metal-free approach

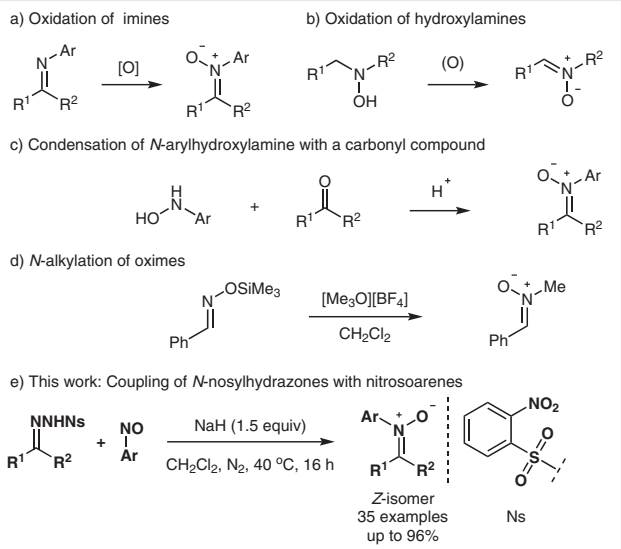
N-Arylnitrones are valuable chemicals[1] that are employed as important intermediates in organic synthesis, acting as electrophile to organometallic compounds and are also used as versatile 1,3-dipoles, which can undergo a variety of organic transformations to give a diverse array of heterocyclic compounds.[2,3] In the past few decades, synthesis of nitrones has received much attention by chemists, because of their diversified applications as building blocks in the synthesis of bioactive compounds, natural products, and stable nitroxyl radicals.[1–4] In addition, some nitrones like 5,5-dimethylpyrroline *N*-oxide (DMPO) and 1,1,3-trimethylisoindole *N*-oxide (TMINO) have served as free radical spin traps in biological systems[5] and are also used as drugs in age-related diseases.[6] There are plenty of methods available for the preparation of nitrones, including the direct oxidation of arylamines/imines (Scheme 1, a),[7] oxidation of hydroxylamines (Scheme 1, b),[8] condensation of hydroxylamines with carbonyl compounds (Scheme 1, c),[9] and N-alkylation/arylation of oximes (Scheme 1, d).[10] However, there are only very few reports available for the one-pot syntheses of nitrones from nitro compounds.[11] More-

Table 1 Optimization of Reaction Conditions[a]



Entry	Base	Yield (%)[b]
1	NaH	98
2	NaH	80[c]
3	NaH	67[d]
4	NaH	54[e]
5	K_2CO_3	58
6	K_3PO_4	46
7	Cs_2CO_3	trace
8	KO*t*-Bu	90
9	LiOMe	88
10	NaOMe	94

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), base (0.75 mmol), and solvent (10 mL) at 40 °C in a sealed tube for 16 h under N_2 atmosphere.
[b] Determined by ^{1}H NMR analysis using CH_2Br_2 (0.5 mmol) as an internal standard. Isolated yield of **3a** from experiment of entry 1 is 90%.
[c] The reaction was run at 40 °C for 4 h under N_2 atmosphere.
[d] AgOTf (20 mol%) was used as the catalyst.
[e] $Cu(OTf)_2$ (20 mol%) was used as the catalyst.

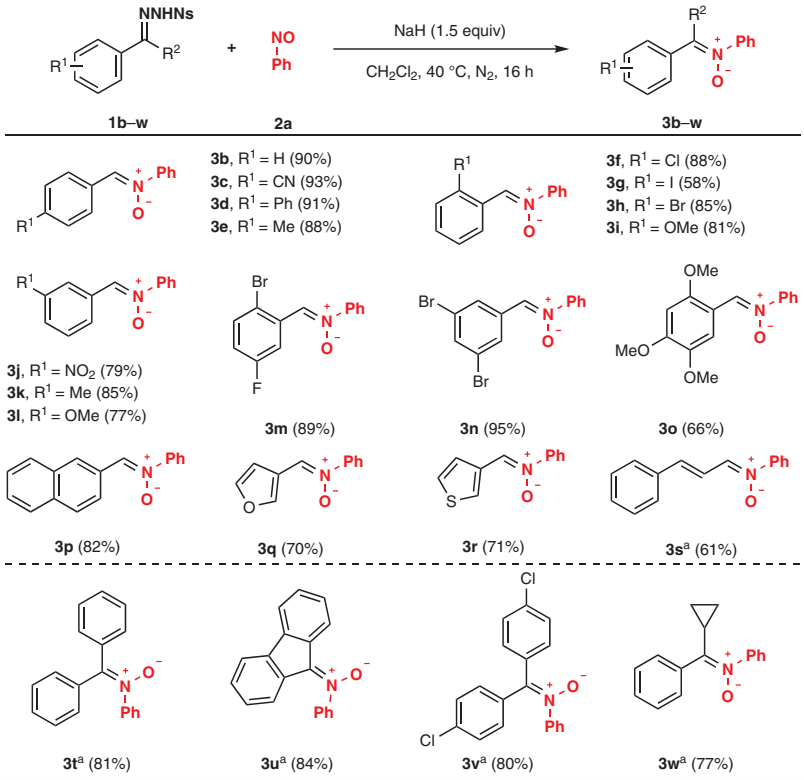


Scheme 1 General strategies for nitrone synthesis

over, a number of protocols have appeared in the literature for the synthesis of aza-heterocycles via in situ generated *N*-arylnitrones from diazo compounds and nitrosoarenes with various dipolarophiles.[12] Huang et al. isolated the *E*-configured oxindole-nitrones from diazooxindoles and nitrosoarenes using silica gel as catalyst under solvent-free conditions.[12i] However, the aforementioned strategies were associated with one or more shortcomings such as harsh reaction conditions, tedious workup procedures, lack of gram-scale preparation, limited substrate scope, and functional group tolerance. In addition, most of the reported methods required transition metal catalysts (Cu, Au/Ag, Ru, or Rh).[12a–e] Therefore, the exploration of an efficient and transition-metal-free protocol to generate *Z*-configured nitrones are highly attractive and most challenging.

Very recently, we studied the low-temperature decomposition of sulfonylhydrazone chemistry, in which *N*-nosylhydrazones were found to be a faster decomposable diazo surrogate than the traditional *N*-tosylhydrazones and successfully utilized them as an alternative diazo precursor in organic transformations.[13] In light of this easy decomposition of *N*-nosylhydrazones under mild conditions to release donor diazo compounds, herein, we wish to establish an efficient and transition-metal-free protocol for the preparation of (*Z*)-*N*-arylnitrones from the one-pot coupling reaction of nitrosoarenes with *N*-nosylhydrazones under mild conditions (Scheme 1, e).

In order to determine the reaction conditions, first a model reaction of *N*-nosylhydrazone **1a** with nitrosobenzene (**2a**) was conducted in the presence of NaH (1.5 equiv) in dichloromethane (10 mL) at 40 °C in a sealed tube

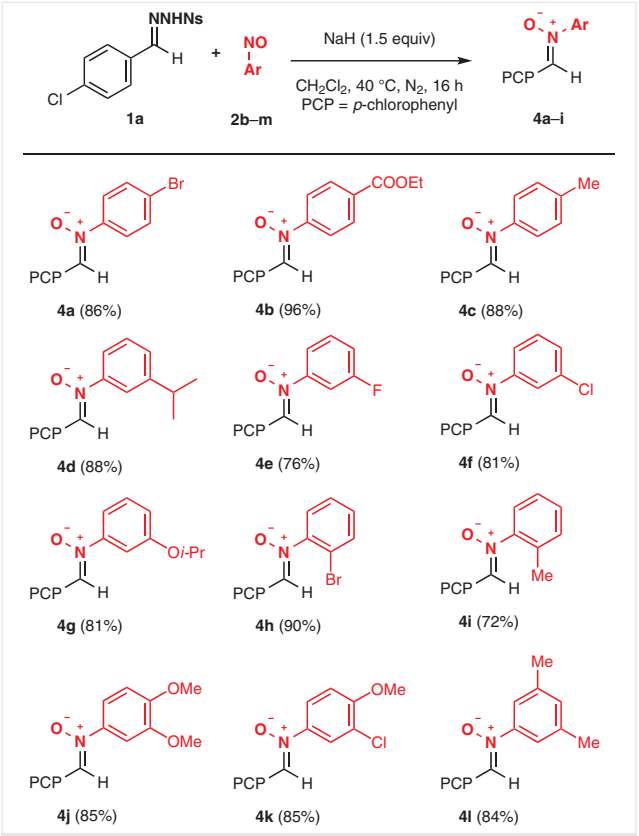


Scheme 2 Scope of *N*-nosylhydrazones. *Reagents and conditions*: **1b–w** (0.5 mmol), **2a** (0.5 mmol), NaH (1.5 equiv), CH_2Cl_2 (10 mL) at 40 °C in a sealed tube for 16 h under N_2 atmosphere. Isolated yields are shown. [a] Reaction was carried out at 50 °C for 16 h.

for 16 hours under nitrogen atmosphere. The corresponding nitrone **3a** was formed in 98% NMR yield (Table 1, entry 1) and the structure was confirmed by its single crystal X-ray crystallographic analysis as *Z*-configuration. In addition, when the same reaction was stopped after 4 hours the nitrone **3a** was formed in 80% yield (entry 2). On the other hand, when we introduced 20 mol% of a transition metal catalyst [AgOTf or $Cu(OTf)_2$] into the reaction mixture, the product yield was diminished to 67% and 54%, respectively (entries 3 and 4), implying that the transition metal salts are not suitable for this coupling reaction. Other inorganic bases (K_2CO_3, K_3PO_4, and Cs_2CO_3) were tested in this reaction, which provided moderate yields of nitrone **3a** (entries 5–7). Some other strong bases like KO*t*-Bu, MeOLi, and MeONa also showed a better efficiency, securing very good yields of final product **3a** (entries 8–10). Based on our model studies, we concluded that NaH (1.5 equiv) and dichloromethane at 40 °C were optimum for this coupling reaction.

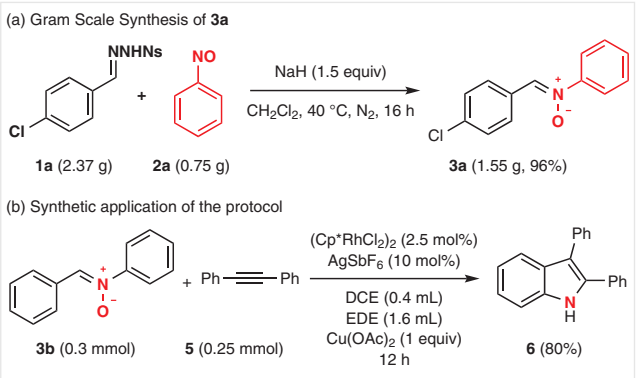
Then, the above optimized reaction conditions were used to assess the substrate scope of *N*-nosylhydrazones and the results are shown in Scheme 2. In this regard, *N*-nosylhydrazones with both electron-rich and electron-deficient functional groups located at any position on the aromatic ring reacted efficiently with nitrosobenzene (**2a**) and the corresponding nitrones **3b–f** and **3h–l** were isolated in good to excellent yields (77–93%) without any column purifications; a single exception was the nitrone **3g** where the yield was slightly lower (58%). As evidenced from the reported results, we assumed that the reaction was not affected by electronic effects. Then, the reaction was further extended to polysubstituted aromatic *N*-nosylhydrazones. In all cases, the desired products were obtained in excellent yields (**3m**, **3n**, and **3o**: 89%, 95% and 66%, respectively). It is worth mentioning that the naphthyl- and heterocyclic-functionalized *N*-nosylhydrazones were also excellent candidates for this reaction, yielding the desired nitrones **3p–r** in very good yields (70–82%). The presence of unsaturation within the *N*-nosylhydrazone structure was not detrimental for the reaction, thus the cinnamyl-substituted compound **1s** also tolerated the reaction at 50 °C to provide the nitrone **3s** in 61% yield. Finally, ketone derived *N*-nosylhydrazones, where the *N*-nosylhydrazones derived from both symmetrical and unsymmetrical ketones were also compatible with the optimized reaction conditions at 50 °C and furnished the corresponding nitrones **3t**, **3v**, and **3w** in 81%, 80% and 77% yield, respectively. More interestingly, *N*-nosylhydrazone derived from fused cyclic ketone **2u** was also nicely tolerated and provided the nitrone **3u** in 84% yield.

Subsequently, the substrate scope was further expanded to various substituted nitrosobenzenes **2b–m** and the results are summarized in Scheme 3. As shown in Scheme 3, nitrosobenzenes having different functional groups (electro- donating, electron-withdrawing, and halogens) in different positions of the benzene ring reacted very well with **1a**, thus providing the desired nitrones **4a–l** in good to excellent yields (72–96%). Not surprisingly, 3,4-dimethoxy-, 3-chloro-4-methoxy-, and 3,5-dimethyl-substituted nitrosobenzenes also reacted well with *N*-nosylhydrazone **1a**, giving the desired nitrones **4j–l** in 84–85% yields. From the nitrosobenzene side, the results also suggested that no electronic factors were involved in the outcome of this protocol. The presence of halogens such as F, Cl, and Br in the nitrone structures deserves much attention because they are significant precursors for a wide variety of transition-metal-catalyzed organic transformations.[14]



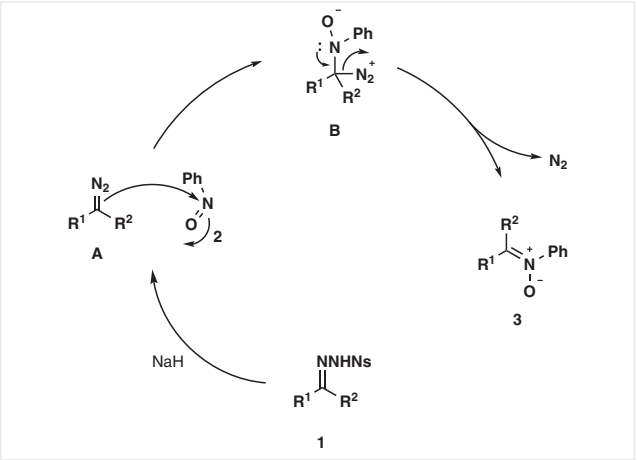
Scheme 3 Scope of nitrosobenzenes. *Reagents and conditions*: **1a** (0.5 mmol), **2b–m** (0.5 mmol), NaH (1.5 equiv) in CH_2Cl_2 (10 mL) at 40 °C in a sealed tube for 16 h under N_2 atmosphere. Isolated yields are shown.

In order to verify the suitability of this protocol to organic preparations, a gram scale reaction of **1a** (2.37 g) with nitrosobenzene **2a** (0.75 g) was conducted by using the standardized conditions, afforded the corresponding nitrone **3a** in 96% yield (1.55 g, Scheme 4). To evaluate the synthetic utility of the synthesized nitrones, we successfully synthesized 2,3-diphenyl-1*H*-indole (**6**) in good yield (80%) via the domino 1,3-dipolar cycloaddition and hetero-Cope rearrangement reaction of nitrone **3b** with 1,2-biphenylacetylene **5**. These multi-functionalized indoles are quite relevant intermediates in the synthesis of natural products and biologically interesting compounds.[15]



Scheme 4 Gram-scale synthesis and synthetic application

Based on the above experimental and previously reported results,[12i,13] a tentative reaction mechanism for the formation of nitrones is proposed as shown in Scheme 5. Initially, the *N*-nosylhydrazone **1** is decomposed by NaH to generate diazo species[13] **A**, which then reacts with nitrosobenzene **2** to form the intermediate **B**. Later, this intermediate **B** undergoes denitrogenation by electron-pushing from the nitrogen lone pair, providing the desired nitrone **3**.



Scheme 5 Plausible mechanism

In summary, we have disclosed an efficient and straightforward approach for the preparation of (*Z*)-*N*-arylnitrones from readily available *N*-nosylhydrazones and nitrosoarenes without the aid of any transition-metal reagent/catalyst. A series of (*Z*)-*N*-arylnitrones have been synthesized in good to excellent yields by simple recrystallization process. The key features of this methodology are mild reaction conditions, simple operation, broad substrate scope, excellent functional group tolerance, and scalability (upto 2.37 g). Thus, this gives an alternative way to access *Z*-configured nitrones.

All reagents were purchased from commercial sources and used without purification, unless otherwise mentioned. The products were purified by recrystallization or column chromatography over silica gel (100–200 size). ^{1}H and ^{13}C NMR spectra were recorded at 25 °C on Varian 600 MHz and 150 MHz or on Bruker 400 MHz and 100 MHz spectrometers and TMS was used as the internal standard. Mass spectra were recorded on Bruker AutoflexIIISmartbeam MS mass spectrometer. High-resolution mass spectra (HRMS) were recorded on Bruker micrOTOF mass spectrometer by using ESI method.

For the preparation of *N*-nosylhydrazones **1a–w** and nitrosobenzenes **2b–m**, see the Supporting Information.

Details of the X-ray crystal data for **3a**[16] are provided in the Supporting Information.

(*Z*)-*N*-(4-Chlorobenzylidene)aniline Oxide (3a); Typical Procedure

A flame-dried sealed tube was charged with *N*-nosylhydrazone **1a** (169.5 mg, 0.5 mmol, 1.0 equiv), NaH (30.0 mg, 60% wt, 0.75 mmol, 1.5 equiv), and nitrosobenzene (**2a**; 53.5 mg, 0.5 mmol, 1.0 equiv). After degassing and refilling with N_2, the tube was charged with anhyd CH_2Cl_2 (10.0 mL, 0.05 M) via syringe. Then the resulting mixture was stirred at 40 °C for 16 h. When the reaction was complete, the crude reaction mixture was cooled to r.t., filtered through a short pad of silica gel with EtOAc as an eluent, and evaporated under vacuum. The crude product was recrystallized from EtOAc/PE to afford pure **3a** as a yellow solid; yield: 103.9 mg (90%); mp 150–151 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 8.4 Hz, 2 H), 7.90 (s, 1 H), 7.75–7.74 (m, 2 H), 7.47–7.41 (m, 5 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.8, 136.2, 133.3, 130.08, 130.03, 129.14, 129.10, 128.8, 121.6.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{11}ClNO$: 232.0524; found: 232.0533.

(*Z*)-*N*-Benzylideneaniline Oxide (3b)

Yield: 88.7 mg (90%); white solid; mp 104–105 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.41–8.39 (m, 2 H), 7.92 (s, 1 H), 7.79–7.77 (m, 2 H), 7.49–7.46 (m, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.1, 134.6, 130.9, 130.7, 129.9, 129.1, 129.0, 128.6, 121.7.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{12}NO$: 198.0913; found: 198.0920.

(*Z*)-*N*-(4-Cyanobenzylidene)aniline Oxide (3c)

Yield: 103.2 mg (93%); white solid; mp 135–136 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.48 (d, *J* = 8.4 Hz, 2 H), 8.00 (s, 1 H), 7.78–7.74 (m, 4 H), 7.52–7.51 (m, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.9, 134.4, 132.7, 132.4, 130.6, 129.4, 128.8, 121.7, 118.5, 113.4.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{11}N_2O$: 223.0866; found: 223.0873.

(*Z*)-*N*-([1,1′-Biphenyl]-4-ylmethylene)aniline Oxide (3d)

Yield: 124.2 mg (91%); yellow solid; mp 183–184 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.48 (d, *J* = 8.4 Hz, 2 H), 7.97 (s, 1 H),7.80 (d, *J* = 7.2 Hz, 2 H), 7.73 (d, *J* = 8.4 Hz, 2 H), 7.66 (d, *J* = 7.2 Hz, 2 H), 7.50–7.45 (m, 5 H), 7.39 (t, *J* = 7.2 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.1, 143.2, 140.1, 134.1, 129.9, 129.6, 129.5, 129.1, 128.9, 127.9, 127.14, 127.05, 121.7.

HRMS (ESI$^+$): m/z [M + H]$^+$ calcd for $C_{19}H_{16}NO$: 274.1226; found: 274.1222.

(*Z*)-*N*-(4-Methylbenzylidene)aniline Oxide (3e)

Yield: 92.8 mg (88%); white solid; mp 90–91 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 7.8 Hz, 2 H), 7.89 (s, 1 H), 7.77 (d, *J* = 7.2 Hz, 2 H), 7.49–7.45 (m, 3 H), 7.29 (d, *J* = 7.8 Hz, 2 H), 2.42 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.1, 141.6, 134.6, 129.7, 129.4, 129.1, 128.1, 121.7, 21.8.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{14}H_{13}NONa$: 234.0891; found: 234.0892.

(*Z*)-*N*-(2-Chlorobenzylidene)aniline Oxide (3f)

Yield: 101.6 mg (88%); white solid; mp 96–97 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.52 (dd, *J* = 7.8, 1.8 Hz, 1 H), 8.41 (s, 1 H), 7.78–7.77 (m,1 H), 7.49–7.43 (m, 4 H), 7.39 (t, *J* = 7.8 Hz, 1 H), 7.34 (td, *J* = 7.8, 1.8 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.3, 133.5, 131.4, 130.2, 130.1, 129.4, 129.1, 129.0, 128.2, 127.1, 121.7.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{13}H_{10}ClNONa$: 254.0343; found: 254.0344.

(*Z*)-*N*-(2-Iodobenzylidene)aniline Oxide (3g)

Yield: 93.6 mg (58%); white solid; mp 94–95 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.43 (dd, *J* = 8.4, 1.2 Hz, 1 H), 8.31 (s, 1 H), 7.80 (d, *J* = 7.8 Hz, 1 H), 7.81–7.80 (m, 2 H), 7.52–7.47 (m, 4 H), 7.12 (td, *J* = 8.4, 1.2 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.1, 139.6, 137.9, 132.3, 131.8, 130.0, 129.13, 129.08, 128.3, 121.6, 100.1.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{13}H_{10}INONa$: 345.9699; found: 345.9705.

(*Z*)-*N*-(2-Bromobenzylidene)aniline Oxide (3h)

Yield: 116.5 mg (85%); yellow solid; mp 97–98 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.50 (dd, *J* = 8.4, 1.2 Hz, 1 H), 8.41 (s, 1 H), 7.78 (dd, *J* = 8.4, 1.2 Hz, 2 H), 7.63 (dd, *J* = 8.4, 1.2 Hz, 1 H), 7.50–7.46 (m, 3 H), 7.43 (t, *J* = 7.8 Hz, 1 H), 7.26 (td, *J* = 7.8, 1.8 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.3, 132.9, 132.8, 131.6, 130.1, 129.6, 129.3, 129.1, 127.6, 124.0, 121.6.

HRMS (ESI$^+$): m/z [M + H]$^+$ calcd for $C_{13}H_{11}BrNO$: 276.0019; found: 276.0025.

(*Z*)-*N*-(2-Methoxybenzylidene)aniline Oxide (3i)

Yield: 91.9 mg (81%); white solid; mp 89–90 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.48 (dd, *J* = 7.8, 1.2 Hz, 1 H), 8.37 (s, 1 H), 7.75 (d, *J* = 7.2 Hz, 2 H), 7.44–7.37 (m, 4 H), 7.06 (t, *J* = 7.2 Hz, 1 H), 6.88 (d, *J* = 7.8 Hz, 1 H), 3.83 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 157.3, 149.4, 132.0, 129.4, 129.1, 128.9, 128.5, 121.6, 120.6, 119.7, 109.7, 55.4.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{14}H_{13}NO_2Na$: 250.0838; found: 250.0844.

(*Z*)-*N*-(3-Nitrobenzylidene)aniline Oxide (3j)

Yield: 95.6 mg (79%); white solid; mp 138–139 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.20 (s, 1 H), 8.79 (d, *J* = 8.4 Hz, 1 H), 8.28 (dd, *J* = 8.4, 1.2 Hz, 1 H), 8.08 (s, 1 H), 7.79–7.78 (m, 2 H), 7.65 (t, *J* = 8.4 Hz, 1 H), 7.51–7.50 (m, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.7, 148.3, 133.8, 132.05, 132.03, 130.6, 129.7, 129.3, 124.9, 123.4, 121.6.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{13}H_{10}N_2O_3Na$: 265.0584; found: 265.0596.

(*Z*)-*N*-(3-Methylbenzylidene)aniline Oxide (3k)

Yield: 89.7 mg (85%); white solid; mp 91–92 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.32 (s, 1 H), 8.11 (d, *J* = 7.8 Hz, 1 H), 7.88 (s, 1 H), 7.75 (dd, *J* = 7.8, 1.2 Hz, 2 H), 7.47–7.44 (m, 3 H), 7.36 (t, *J* = 7.8 Hz, 1 H), 7.27 (d, *J* = 7.8 Hz, 1 H), 2.41 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.0, 138.2, 134.7, 131.8, 130.5, 129.8, 129.3, 129.0, 128.4, 126.4, 121.6, 21.4.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{14}H_{13}NONa$: 234.0889; found: 234.0891.

(*Z*)-*N*-(3-Methoxybenzylidene)aniline Oxide (3l)

Yield: 87.4 mg (77%); white solid; mp 91–92 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.37–8.36 (m, 1 H), 7.90 (s, 1 H), 7.76–7.74 (m, 2 H), 7.65 (d, *J* = 7.8 Hz, 1 H), 7.46–7.43 (m, 3 H), 7.34 (t, *J* = 7.8 Hz, 1 H), 7.01 (dd, *J* = 8.4, 2.4 Hz, 1 H), 3.86 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.5, 148.9, 134.5, 131.8, 129.8, 129.3, 129.0, 122.1, 121.6, 117.8, 112.5, 55.2.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{14}H_{13}NO_2Na$: 250.0838; found: 250.0847.

(*Z*)-*N*-(2-Bromo-5-fluorobenzylidene)aniline Oxide (3m)

Yield: 130.4 mg (89%); yellow solid; mp 144–145 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.34 (dd, *J* = 10.8, 3.0 Hz, 1 H), 8.39–8.38 (m, 1 H), 7.78–7.76 (m, 2 H), 7.60–7.57 (m, 1 H), 7.50–7.47 (m, 3 H), 7.03–7.00 (m, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.5 (d, *J* = 244.5 Hz), 149.2, 133.7 (d, *J* = 7.5 Hz), 132.2, 131.0 (d, *J* = 10.5 Hz), 130.4, 129.2, 121.6, 118.6 (d, *J* = 24.0 Hz), 118.0 (d, *J* = 3.0 Hz), 116.2 (d, *J* = 28.5 Hz).

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{13}H_9BrFNONa$: 315.9744; found: 315.9752.

(*Z*)-*N*-(3,5-Dibromobenzylidene)aniline Oxide (3n)

Yield: 168.6 mg (95%); white solid; mp 90–91 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.51–8.50 (m, 2 H), 7.85 (s, 1 H), 7.74–7.73 (m, 3 H), 7.50–7.49 (m, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.8, 135.8, 133.7, 131.6, 130.5, 129.8, 129.3, 123.1, 121.6.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{13}H_9Br_2NONa$: 375.8943; found: 375.8935.

(*Z*)-*N*-(2,4,5-Trimethoxybenzylidene)aniline Oxide (3o)

Yield: 94.7 mg (66%); white solid; mp 134–135 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.30 (s, 1 H), 8.31 (s, 1 H), 7.77 (d, *J* = 7.2 Hz, 2 H), 7.46–7.41 (m, 3 H), 6.51 (s, 1 H), 3.948 (s, 3 H), 3.942 (s, 3 H), 3.87 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.7, 152.0, 149.2, 142.2, 129.4, 129.3, 129.0, 121.5, 112.0, 111.2, 95.6, 56.3, 56.1, 55.9.

HRMS (ESI$^+$): m/z [M + Na]$^+$calcd for $C_{16}H_{17}NO_4Na$: 310.1050; found: 310.1058.

(*Z*)-*N*-(Naphthalen-2-ylmethylene)aniline Oxide (3p)

Yield: 101.3 mg (82%); white solid; mp 118–119 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.44 (s, 1 H), 8.07 (s, 1 H), 8.01 (dd, *J* = 8.4, 1.2 Hz, 1 H), 7.97 (d, *J* = 7.8 Hz, 1 H), 7.87 (d, *J* = 8.4 Hz, 1 H), 7.84–7.82 (m, 3 H), 7.55–7.47 (m, 5 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.0, 134.5, 134.3, 133.1, 129.9, 129.3, 129.12, 129.06, 128.0, 127.8, 127.6, 127.5, 126.5, 126.1, 121.7.

HRMS(ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{17}H_{13}NONa$: 270.0889; found: 270.0898.

(*Z*)-*N*-(Furan-3-ylmethylene)aniline Oxide (3q)

Yield: 65.5 mg (70%); white solid; mp 92–93 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.12 (s, 1 H), 7.94 (s, 1 H), 7.78–7.76 (m, 2 H), 7.51 (t, *J* = 1.8 Hz, 1 H), 7.49–7.45 (m, 3 H), 6.66 (d, *J* = 1.8 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 147.4, 146.8, 143.0, 129.8, 129.2, 127.3, 121.3, 117.3, 109.6.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{11}H_9NO_2Na$: 210.0525; found: 210.0530.

(*Z*)-*N*-(Thiophen-3-ylmethylene)aniline Oxide (3r)

Yield: 72.1 mg (71%); white solid; mp 96–97 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.16 (d, *J* = 3.0 Hz, 1 H), 8.06 (s, 1 H), 7.79–7.78 (m, 2 H), 7.50–7.45 (m, 4 H), 7.39–7.38 (m, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.2, 131.6, 129.9, 129.8, 129.2, 129.0, 128.1, 125.4, 121.5.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{11}H_9SNONa$: 226.0297; found: 226.0301.

(*Z*)-*N*-[(*E*)-4-Phenylbut-3-en-1-ylidene]aniline Oxide (3s)

Yield: 68.0 mg (61%); yellow solid; mp 144–145 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 9.6 Hz, 1 H), 7.75–7.74 (m, 2 H), 7.70 (dd, *J* = 16.2, 9.6 Hz, 1 H), 7.55 (d, *J* = 7.2 Hz, 2 H), 7.44–7.43 (m, 3 H), 7.37–7.31 (m, 3 H), 7.15 (d, *J* = 16.2 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 147.3, 139.8, 136.1, 136.0, 129.9, 129.4, 129.0, 128.8, 127.4, 121.3, 119.0.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{15}H_{13}NONa$: 246.0889; found: 246.0880.

***N*-(Diphenylmethylene)aniline Oxide (3t)**

Yield: 110.6 mg (81%); yellow solid; mp 199–200 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.06–8.05 (m, 2 H), 7.41–7.40 (m, 3 H), 7.31–7.29 (m, 2 H), 7.24–7.19 (m, 6 H), 7.11–7.10 (m, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.5, 135.7, 134.1, 131.1, 130.5, 130.1, 128.7, 128.6, 128.5, 128.2, 127.9, 124.6.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{19}H_{15}NONa$: 296.1046; found: 296.1050.

***N*-(9*H*-Fluoren-9-ylidene)aniline Oxide (3u)**

Yield: 114.2 mg (84%); yellow solid; mp 166–167 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.93 (d, *J* = 7.8 Hz, 1 H), 7.71 (d, *J* = 7.8 Hz, 1 H), 7.65 (d, *J* = 7.2 Hz, 1 H), 7.62–7.60 (m, 3 H), 7.54–7.51 (m, 2 H), 7.50 (td, *J* = 7.2, 1.2 Hz, 1 H), 7.44 (td, *J* = 7.2, 1.2 Hz, 1 H), 7.26–7.25 (m, 1 H), 6.91–6.88 (m, 1 H), 5.90 (d, *J* = 7.8 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 147.1, 145.5, 139.3, 139.1, 132.4, 131.2, 130.8, 130.3, 130.2, 129.2, 128.9, 127.3, 127.1, 123.8, 120.2, 119.6.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{19}H_{13}NONa$: 294.0889; found: 294.0893.

***N*-[Bis(4-chlorophenyl)methylene]aniline Oxide (3v)**

Yield: 136.4 mg (80%); yellow solid; mp 199–200 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 9.0 Hz, 2 H), 7.38 (d, *J* = 8.4 Hz, 2 H), 7.27–7.25 (m, 5 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 7.03(d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.1, 145.3, 135.9, 135.1, 133.6, 132.4, 132.2, 131.7, 129.0, 128.9, 128.8, 128.3, 124.4.

HRMS (ESI$^+$): m/z [M + H]$^+$ calcd for $C_{19}H_{14}Cl_2NO$: 342.0452; found: 342.0446.

(*Z*)-*N*-[Cyclopropyl(phenyl)methylene]aniline Oxide (3w)

Yield: 91.2 mg (77%); yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.21–7.20 (m, 2 H), 7.18–7.11 (m, 6 H), 7.00–6.97 (m, 2 H), 3.15–3.11 (m, 1 H), 1.13–1.10 (m, 2 H), 0.60–0.58 (m, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 147.0, 131.0, 130.0, 128.8, 128.6, 128.3, 128.1, 124.5, 123.8, 13.6, 6.5.

HRMS (ESI$^+$): m/z [M + H]$^+$ calcd for $C_{16}H_{16}NO$: 238.1226; found: 238.1235.

(*Z*)-4-Bromo-*N*-(4-chlorobenzylidene)aniline Oxide (4a)

Yield: 133.3 mg (86%); yellow solid; mp 144–145 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 9.0 Hz, 2 H), 7.87 (s, 1 H), 7.63 (d, *J* = 9.0 Hz, 2 H), 7.58 (d, *J* = 9.6 Hz, 2 H), 7.42 (d, *J* = 9.0 Hz, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 147.6, 136.6, 133.2, 132.2, 130.1, 128.9, 128.8, 124.0, 123.1.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{13}H_{10}BrClNO$: 309.9629; found: 309.9618.

(*Z*)-*N*-(4-Chlorobenzylidene)-4-(ethoxycarbonyl)aniline Oxide (4b)

Yield: 145.4 mg (96%); yellow solid; mp 117–118 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.37 (d, *J* = 8.4 Hz, 2 H), 8.17 (d, *J* = 9.0 Hz, 2 H), 7.96 (s, 1 H), 7.85 (d, *J* = 8.4 Hz, 2 H), 7.46 (d, *J* = 9.0 Hz, 2 H), 4.41 (q, *J* = 7.2 Hz, 2 H), 1.42 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR(150 MHz, $CDCl_3$): δ = 165.2, 151.6, 136.8, 133.9, 132.0, 130.6, 130.3, 129.0, 128.8, 121.6, 61.5, 14.2.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{16}H_{15}ClNO_3$: 304.0735; found: 304.0730.

(*Z*)-*N*-(4-Chlorobenzylidene)-4-methylaniline Oxide (4c)

Yield: 107.8 mg (88%); yellow solid; mp 166–167 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.35 (d, *J* = 8.4 Hz, 2 H), 7.89 (s, 1 H), 7.65 (d, *J* = 8.4 Hz, 2 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 7.27 (d, *J* = 7.8 Hz, 2 H), 2.42 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 146.7, 140.4, 136.2, 132.8, 130.1, 129.7, 129.3, 128.9, 121.4, 21.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{13}ClNO$: 246.0680; found: 246.0685.

(*Z*)-*N*-(4-Chlorobenzylidene)-4-isopropylaniline Oxide (4d)

Yield: 120.1 mg (88%); yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 9.0 Hz, 2 H), 7.89 (s, 1 H), 7.65 (s, 1 H), 7.51 (d, *J* = 7.8 Hz, 1 H), 7.43 (d, *J* = 9.0 Hz, 2 H), 7.38 (t, *J* = 7.8 Hz, 1 H), 7.32 (d, *J* = 7.8 Hz, 1 H), 3.01–2.97 (m, 1 H), 1.28 (d, *J* = 6.6 Hz, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.5, 149.0, 136.2, 133.3, 130.1, 129.2, 129.0, 128.9, 128.3, 119.9, 118.9, 34.1, 23.8.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{17}ClNO$: 274.0993; found: 274.0983.

(*Z*)-*N*-(4-Chlorobenzylidene)-3-fluoroaniline Oxide (4e)

Yield: 94.6 mg (76%); white solid; mp 100–101 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.35 (d, *J* = 9.0 Hz, 2 H), 7.91 (s, 1 H), 7.57–7.54 (m, 2 H), 7.47–7.443 (m, 3 H), 7.19–7.17 (m, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.6 (d, *J* = 247.5 Hz), 150.0 (d, *J* = 7.5 Hz), 136.7, 133.5, 130.4 (d, *J* = 8.6 Hz), 130.2, 128.9, 128.8, 117.1 (d, *J* = 21.4 Hz), 117.0 (d, *J* = 3.6 Hz), 109.8 (d, *J* = 27.0 Hz).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}ClFNO$: 250.0429; found: 250.0432.

(*Z*)-3-Chloro-*N*-(4-chlorobenzylidene)aniline Oxide (4f)

Yield: 107.3 mg (81%); yellow solid; mp 96–97 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.4 Hz, 2 H), 7.88 (s, 1 H), 7.79 (t, *J* = 1.8 Hz, 1 H), 7.65–7.63 (m, 1 H), 7.44–7.41 (m, 3 H), 7.39 (t, *J* = 8.4 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.6, 136.6, 135.0, 133.5, 130.20, 130.16, 128.9, 128.8, 122.2, 119.7.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}Cl_2NO$: 266.0134; found: 266.0131.

(*Z*)-*N*-(4-Chlorobenzylidene)-3-isopropoxyaniline Oxide (4g)

Yield: 117.0 mg (81%); yellow solid; mp 117–118 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 8.4 Hz, 2 H), 7.90 (s, 1 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 7.35–7.32 (m, 2 H), 7.25–7.24 (m, 1 H), 6.99–6.97 (m, 1 H), 4.64–4.60 (m, 1 H), 1.36 (d, *J* = 6.0 Hz, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 158.6, 150.1, 136.3, 133.3, 130.2, 129.8, 129.1, 128.9, 117.9, 113.2, 109.2, 70.5, 21.9.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}ClNO$: 290.0942; found: 290.0948.

(*Z*)-2-Bromo-*N*-(4-chlorobenzylidene)aniline Oxide (4h)

Yield: 140.0 mg (90%); yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 8.4 Hz, 2 H), 7.68 (dd, *J* = 8.4, 1.2 Hz, 1 H), 7.58 (dd, *J* = 7.8, 1.8 Hz, 1 H), 7.54 (s, 1 H), 7.46–7.42 (m, 3 H), 7.33 (td, *J* = 7.8, 1.8 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.1, 137.6, 136.8, 133.9, 130.8, 130.2, 129.0, 128.5, 128.4, 125.6, 116.4.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}BrClNO$: 309.9629; found: 309.9604.

(*Z*)-*N*-(4-Chlorobenzylidene)-2-methylaniline Oxide (4i)

Yield: 88.2 mg (72%); white solid; mp 137–138 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 7.8 Hz, 2 H), 7.55 (s, 1 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 7.39–7.26 (m, 4 H), 2.42 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.6, 136.33, 136.29, 131.7, 131.5, 129.9, 129.5, 128.91, 128.87, 126.7, 123.3, 17.0.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{13}ClNO$: 246.0680; found: 246.0688.

(*Z*)-*N*-(4-Chlorobenzylidene)-3,4-dimethoxyaniline Oxide (4j)

Yield: 123.6 mg (85%); white solid; mp 130–131 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.35 (d, *J* = 9.0 Hz, 1 H), 7.88 (s, 1 H), 7.44–7.42 (m, 3 H), 7.23 (dd, *J* = 9.0, 2.4 Hz, 1 H), 6.86 (d, *J* = 8.4 Hz, 1 H), 3.94 (s, 3 H), 3.93 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.4, 149.3, 142.4, 136.2, 132.6, 130.1, 129.3, 128.9, 113.1, 110.1, 105.7, 56.18, 56.16.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{14}ClNO_3Na$: 314.0554; found: 314.0554.

(*Z*)-3-Chloro-*N*-(4-chlorobenzylidene)-4-methoxyaniline Oxide (4k)

Yield: 125.4 mg (85%); white solid; mp 141–142 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.4 Hz, 2 H), 7.84–7.83 (m, 2 H), 7.68 (dd, *J* = 8.4, 2.4 Hz, 1 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 6.98 (d, *J* = 8.4 Hz, 1 H), 3.96 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 156.3, 142.1, 136.4, 132.7, 130.1, 129.0, 128.9, 123.7, 122.9, 121.0, 111.5, 56.5.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{12}Cl_2NO_2$: 296.0290; found: 296.0286.

(*Z*)-*N*-(4-Chlorobenzylidene)-3,5-dimethylaniline Oxide (4l)

Yield: 108.8 mg (84%); yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 9.0 Hz, 2 H), 7.86 (s, 1 H), 7.42 (d, *J* = 8.4 Hz, 2 H), 7.35 (s, 2 H), 7.08 (s, 1 H), 2.38 (s, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.0, 139.1, 136.1, 133.2, 131.6, 130.1, 129.3, 128.8, 119.4, 21.2.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{15}ClNO$: 260.0837; found: 260.0843.

Gram-Scale Synthesis of 3a

The typical procedure was followed, but the reaction was conducted on a 7 mmol scale. *N*-Nosylhydrazone **1a** (2.37 g, 7.0 mmol, 1.0 equiv), 60% NaH (420 mg, 12 mmol, 1.5 equiv), nitrosobenzene (**2a**; 0.75 g, 7.0 mmol, 1.0 equiv) and CH_2Cl_2 (120 mL) were mixed under N_2 atmosphere in a flame-dried sealed tube in a glovebox. Then the reaction mixture was stirred at 40 °C for 24 h. After completion, the mixture was filtered and evaporated under reduced pressure to give the crude product. Finally, the crude product was recrystallized from petroleum ether to afford the pure **3a** as a yellow solid; yield: 1.55 g (96%).

2,3-Diphenyl-1*H*-indole (6)

The indole **6** was prepared according to the literature procedure.[17] $[Cp^*RhCl_2]_2$ (3.9 mg, 0.00625 mmol, 2.5 mol %), $AgSbF_6$ (8.6 mg, 0.025 mmol, 10 mol %), and $Cu(OAc)_2$ (45.4 mg, 0.25 mmol, 1.0 equiv) were weighed in a glove-box and placed in a dried Schlenk tube. Then, the solvent mixture DCE/EDE (EDE=1,2-diethoxyethane) (2 mL, 1:4, v/v)

was added and the mixture was stirred at r.t. for 30 min. Then nitrone **3b** (59 mg, 0.3 mmol, 1.2 equiv) was added followed by tolane (**5**; 45 mg, 0.25 mmol, 1.0 equiv). The resulting mixture was stirred at 100 °C for 12 h. After cooling to r.t., the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EtOAc to afford the desired product **6** as a fluorescent yellow liquid; yield: 53.8 mg (80%).

^{1}H NMR (600 MHz, CDCl3): δ = 8.12 (s, 1 H), 7.60 (d, *J* = 7.8 Hz, 1 H), 7.37–7.33 (m, 5 H), 7.27 (t, *J* = 7.8 Hz, 2 H), 7.25–7.19 (m, 4 H), 7.18–7.15 (m, 1 H), 7.07 (t, *J* = 7.2 Hz, 1 H).

^{13}C NMR (150 MHz, CDCl3): δ = 135.9, 135.0, 134.1, 132.7, 130.1, 128.75, 128.67, 128.51, 128.2, 127.7, 126.2, 122.7, 120.4, 119.7, 115.1, 110.9.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{16}N$: 270.3490; found: 270.3495.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591757.

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(16) CCDC 1556499 (**3a**) contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

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