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Preparation of Ketimines from Aryldiazonium Salts, Arenes, and Nitriles via Intermolecular Arylation of *N*-Arylnitrilium Ions

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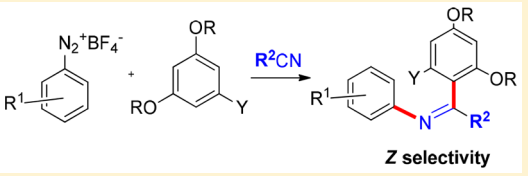
Supporting Information

ABSTRACT: A transition-metal-free approach for the preparation of *N*-arylketimines has been developed from the direct reaction of aryldiazonium salts, arenes, and nitriles in a one-pot fashion with the consecutive formation of N−C and C−C bonds. This approach proceeds via an *in situ* generation of *N*-arylnitrilium intermediate, which then undergoes intermolecular arylation. This three-component strategy offers a step- and atom-efficient way to *N*-arylketimines from easily accessible reagents under mild reaction conditions. The characterization of stereochemistry of ketimine was achieved by X-ray crystallographic structure and theoretical calculation. Operational simplicity, shorter reaction time, excellent functional group compatibility, and scalability are the key features of this report.



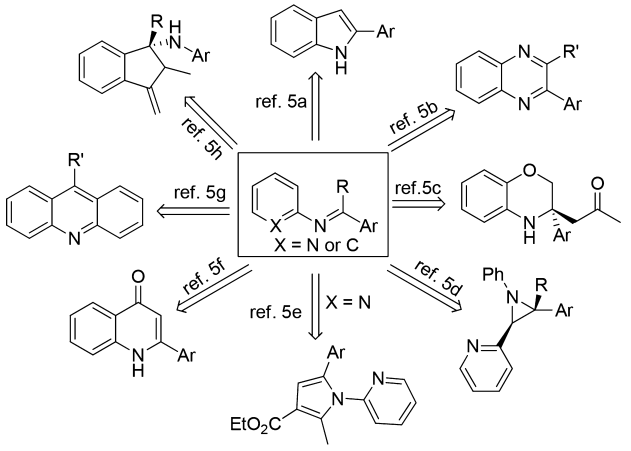
INTRODUCTION

Imines and their derivatives represent a privileged class of *N*-containing compounds and constitutes a major area of research in organic chemistry. They serve as potential intermediates in the synthesis of various *N*-heterocycles, natural products, agrochemicals, fragrances, and dyes.[1] Ketimines are an important subclass of imines that often serve as a versatile electrophile for chiral amines,[2] 1,2-diamines,[3] and α- or β-amino acids via asymmetric addition.[4] Typical examples using *N*-arylketimines as a key precursor in various organic transformation are summarized in Scheme 1.[5] In addition, ketimines are renowned building blocks for the preparation of α-chiral amines[6] and ligands.[7]

To date, several elegant methods have been described for the synthesis of *N*-arylketimines. A well-established method is the direct condensation of the amine with a carbonyl compound often in the presence of a Lewis acid.[8] Other efficient methods include oxidative self-condensation of amines,[9] oxidative coupling of amines and alcohols,[10] hydroamination of alkynes[11] or alkenes,[12] with amines, and tandem Beckmann−electrophilic aromatic substitution (TB-EAS) of benzophenone oximes.[13] In addition, *N*-arylketimines can also be accessed from the reaction of ketones with different reagents such as *N*,*N*-bis(trimethylsilyl)amines,[14a] $PhN(AlCl_2)_2$,[14b] and $ArN(MgBr)_2$.[14c] It has been also reported that *N*-arylketimines can be obtained from an intermolecular coupling of common secondary amides with arenes.[15] Despite the significance, these methods suffer from a number of limitations including the requirement of high-temperature azeotropic distillation, prolonged reaction times, and need for Lewis acid catalysts/dehydrating agents[16] such as $TiCl_4$, Al_2O_3, and Bu_2SnCl_2, which greatly affects sensitive functional groups. To circumvent these issues, a synthetic method from readily available, inexpensive precursors via environmentally benign and transition-metal free conditions is highly desirable.

Aryldiazonium salts are employed widely in organic synthesis due to the high reactivity and ease of preparation. Due to their inherent electrophilicity, coming from N_2 being an excellent leaving group, aryldiazonium salts have been utilized in various transition-metal free organic transformations.[17] In particular, the synthetic application involving *in situ* generation of a nitrilium ion from aryldiazonium and nitrile has received much attention due to the easy handling procedure.[18,19] Approaches for the multisubstituted phenanthridine core from 2-aryldiazonium salts and nitriles were documented via the *in situ* generation of the *N*-arylnitrilium intermediate followed by intramolecular

Scheme 1. Synthetic Importance of *N*-Arylketimines



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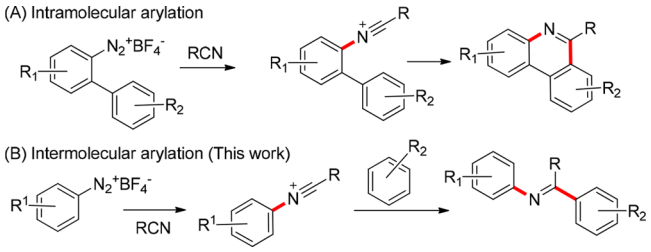
arylation (Scheme 2A).[18a,19a] Inspired by this work and our recent developments on aryldiazonium salts based applications,[19b−e] herein, we disclose a mild and transition-metal-free synthesis of *N*-arylketimines, involving the reaction of the reactive *N*-arylnitrilium intermediate with activated aryl compounds via an intermolecular fashion (Scheme 2B).[20]

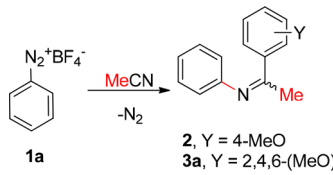
Scheme 2. Inter- *versus* Intramolecular Arylation with Nitrilium Ions



RESULTS AND DISCUSSION

Initially, we carried out the reaction of phenyldiazonium salt with anisole or 1,3,5-trimethoxybenzene in acetonitrile, and the results are summarized in Table 1. In the initial attempt, diazonium salt **1a** reacted with anisole in anhydrous MeCN at room temperature for 12 h (Table 1, entry 1). To our delight, the expected ketimine was obtained in trace amounts. Performing the reaction at 80 °C provided **2** in 26% yield. Upon extending the reaction time to 12 h with 3 equiv of anisole, the yield of **2** increased to 41% (Table 1, entry 3). After significant screening efforts, the use of 1,3,5-trimethoxybenzene led to the desired product **3a** in 87% yield at 80 °C for 2 h (Table 1, entry 5) due to the highly activated aryl ring. Conducting the reaction in the presence of organic solvents such as dichloroethane and toluene resulted in inferior results (Table 1, entries 7−9). It is noticed that, in these reactions, we did not observe any diazo coupling product as the side product, presumably due to the reaction proceeding in a nitrile solution. The use of excess of nitrile does facilitate the formation of the nitrilium ion (entries 7 vs 8). Carrying out the reaction of **1a** with 1,3,5-trimethoxybenzene and CH_3CN in a methanol solution provided majorly the diazo coupling product, 1-phenyl-2-(2,4,6-trimethoxyphenyl)diazene, indicating that this coupling is favored in a polar protic solvent (entry 10).[21]

Table 1. Reaction Optimzation[a]



entry	solvent	arene	T (°C)	t (h)	yield[b]
1	CH_3CN (2 mL)	anisole	rt	12	**2** (trace)
2	CH_3CN (2 mL)	anisole	80	2	**2** (26%)
3[c]	CH_3CN (2 mL)	anisole	80	12	**2** (41%)
4[c]	CH_3CN (2 mL)	anisole	110	3	**2** (31%)
5	CH_3CN (2 mL)	1,3,5-$C_6H_3(OMe)_3$	80	2	**3a** (87%)
6	CH_3CN (2 mL)	1,3,5-$C_6H_3(OMe)_3$	80	12	**3a** (84%)
7[d]	MeCN/$ClCH_2CH_2Cl$	1,3,5-$C_6H_3(OMe)_3$	80	12	**3a** (64%)
8[e]	MeCN/$ClCH_2CH_2Cl$	1,3,5-$C_6H_3(OMe)_3$	80	12	**3a** (21%)
9[d]	MeCN/toluene	1,3,5-$C_6H_3(OMe)_3$	80	12	**3a** (62%)
10	MeCN/MeOH	1,3,5-$C_6H_3(OMe)_3$	65	12	**3a** (0%)[f]

[a]Reaction conditions: a mixture of **1a** (0.52 mmol), arene (0.57 mmol), and MeCN (2 mL) in a reaction tube. [b]Yields given in parentheses were determined by ^{1}H NMR. [c]3 equiv of anisole were used. [d]MeCN (1 mL) in solvent (2 mL). [e]5 equiv of CH_3CN. [f]1-Phenyl-2-(2,4,6-trimethoxyphenyl)diazene as the major product.

Under the optimal conditions, a broad range of substituted aryldiazonium salts were explored as substrates and the results are shown in Table 2. Varieties of aryldiazonium salts participated well in the reaction and furnished the corresponding *N*-arylketimines in good to excellent yields regardless of the position of the substituents. Common functional groups such as ester, keto, ether, and halogens were found to be compatible, and the desired products were obtained in good yields (Table 2, entries **3a**−**3i**). Gratifyingly, fused and multiply substituted aryldiazonium salts were also viable substrates and afforded the desired products in useful yields (Table 2, entries **3k**, **3m**−**3n**). Notably, 2,4,6-trimethylphenyldiazonium salt with sterically distinct substituents delivered **3l** in good yield (59%).

On the other hand, various nitrile components were also utilized and found to be applicable to afford the corresponding products in good yields (Table 3). Alkyl nitriles bearing a 1°, 2°, 3°, or cyclic aliphatic group participated smoothly and furnished the corresponding *N*-arylketimines in good yields (Table 3, entries **4a**−**4d**). To our delight, α-chloroacetonitrile was also amenable for this reaction to furnish the desired compound **4e** in 83% yield. The chloro functionality on the alkyl chain remains intact, thus providing a handle for further chemical transformation. Intriguingly, a series of differently substituted arylnitriles were used in this reaction to deliver diaryl substituted ketimines in yields ranging from 58% to 82% (Table 3, entries **4f**−**4h**). Notably, in the case of **4f**, PhCN was recovered in 86% yield in analytically pure form, thus making the process more sustainable and economic. Moreover, excellent *Z* selectivity was observed in most of the cases as shown. The stereochemistry of imine is confirmed by X-ray crystallographic structure of **4f** and theoretical calculation on the energy difference of *E*−*Z* isomers (see Supporting Information).

The structure of **4f** is depicted in Figure S1. Two independent molecules appear in the unit cell. In both molecules, the *N*-phenyl group is seated *cis* to the trimethoxyphenyl group, resulting in the *Z* configuration of the ketimine product. The distances of C═N are 1.282(2) and 1.287(2) Å, respectively, in agreement with carbon−nitrogen double bonds. Notably, both trimethoxyphenyl and *N*-phenyl substituents of **4f** are bisected to the C═N bond with φ = 66.19° and 72.95° respectively, while the phenyl group at C10 is almost coplanar to the C═N [φ = 3.90°]. These observations are in agreement with the corresponding DFT calculated torsional angles [φ = 58.8°, 10.3°, and 71.9°, respectively]. Table 4 summarizes the energy difference between *E*−*Z* isomers of various ketimines based on the DFT calculations at the B3LYP/6-31+G(d,p) and ωB97X-D/6-31+G(d,p) levels. It appears that the *Z*-isomers of the *ortho* substituted aryl ketimines such **3a**, **4f**, **4d**, and **5f** are more stable than the corresponding *E*-isomers. On the other hand, the *E*-isomeric structure in compound **2** is favored due to the less steric aryl substituent, i.e., the *p*-methoxyphenyl group, which is

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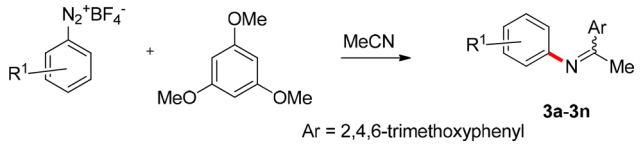
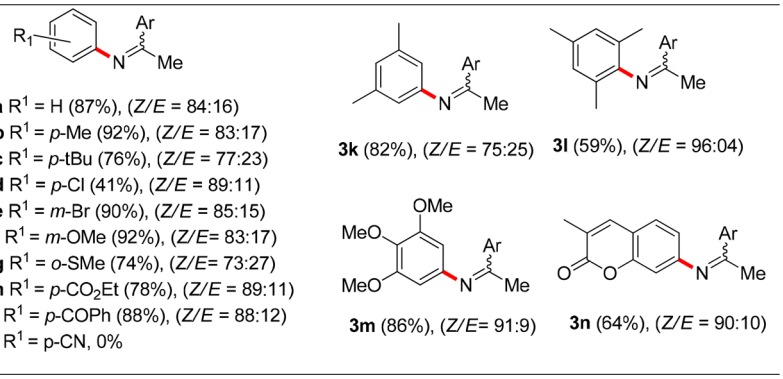
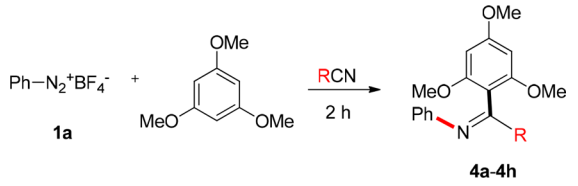
Table 2. Reaction of Various Aryldiazonium Salts with 1,3,5-$C_6H_3(OMe)_3$ in MeCN[a]

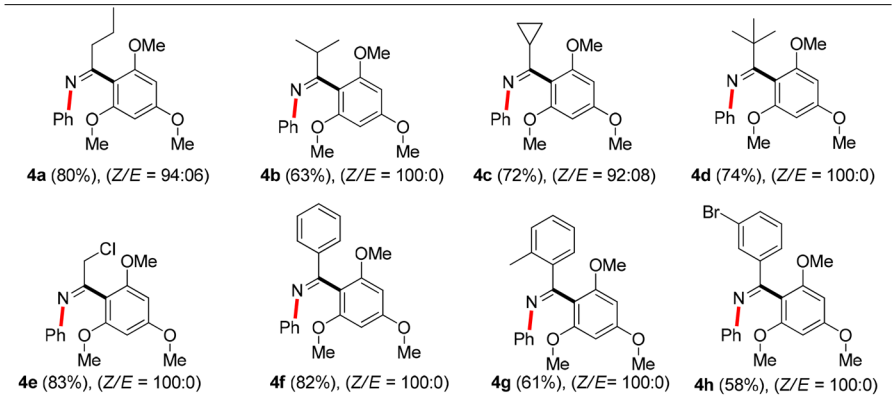




[a]Reaction conditions: diazonium salt (0.52 mmol) and 1,3,5-$C_6H_3(OMe)_3$ (0.57 mmol) in MeCN (2 mL) were heated to 80 °C for 2 h; *E*/*Z* ratios determined by ^{1}H NMR.

Table 3. Reaction of Various Nitriles with 1a and 1,3,5-$C_6H_3(OMe)_3$[a]





[a]Reaction conditions: diazonium salt (0.52 mmol) and 1,3,5-$C_6H_3(OMe)_3$ (0.57 mmol) in RCN (2 mL) were heated to 80 °C for 2 h; *E*/*Z* ratios determined by ^{1}H NMR.

similar to the work reported by Lammertsma's group in pyridine-stabilized nitrilium ions.[20a]

Next, the scope of this method toward various arene components was investigated, and the results are summarized in Table 5. It was noted that arene partners bearing mono-, di-, and trimethoxy substituents were involved in the reaction and led to smooth assembly of multisubstituted *N*-arylketimines in acceptable yields (Table 5, entries **5a**−**5f**). Notably, an excellent *E* selectivity was obtained when anisole was employed as the reaction component, but low yields (**2** and **5a**−**5c**). DFT calculation confirms the *E* configuration of **2** (ΔG_{E-Z} = −2.7 kcal/mol, Table 4), which is also supported by the ^{1}H NMR data of **2** reported by Gschwind's group.[22b] Moreover, 1-bromo-3,5-dimethoxybenzene also participated well in the transformation and provided the halogenated *N*-arylketimine **5g** in excellent yield. Notable flexibility can be exerted, concerning the arene component; thus, mesitylene smoothly participated in the reaction leading to the corresponding *N*-arylketimine in good yields (Table 5, entry **5h**). Preparation of such a diversely functionalized *N*-arylketimine derivative through other known synthetic avenues would be challenging and may require multistep synthesis. Unfortunately, toluene and benzofuran failed to deliver the desired product.

In order to investigate the reactivity outcome of *N*-arylnitrilium intermediate, specific experiments were conducted (Scheme 3). In contrast to our previous observations,[19] aryldiazonium salt **6** reacted with 1,3,5-trimethoxybenzene in acetonitrile to give **7** in excellent yield instead of the formation of 6-methylphenanthridine (Scheme 3a). Seemingly, the rate of intermolecular cyclization of *N*-arylnitrilium intermediate is

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Table 4. Energy Differences of *E,Z* Isomeric Ketimines Based on DFT Calculation

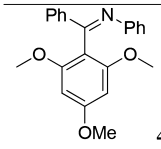
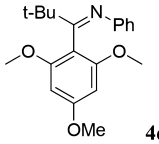
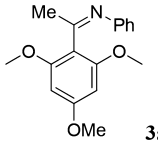
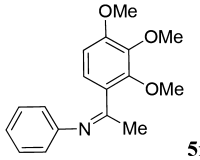
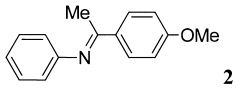
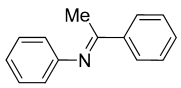
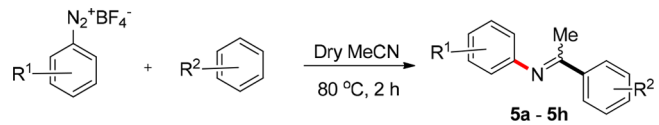
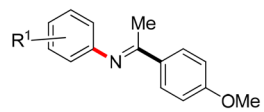
Compound	$\Delta G_{(E\text{-}Z)}$ = B3LYP/6-31+G(d,p)	$\Delta G_{(E\text{-}Z)}$ = ωB97X-D/6-31+G(d,p)	Note
 **4f**	5.6 kcal/mol	5.1 kcal/mol *Z*-isomer favored	this work
 **4d**	6.0 kcal/mol	6.8 kcal/mol *Z*-isomer favored	this work
 **3a**	2.4 kcal/mol	3.2 kcal/mol *Z*-isomer favored	this work
 **5f**	2.1 kcal/mol	2.5 kcal/mol *Z*-isomer favored	this work
 **2**	- 3.6 kcal/mol	- 2.7 kcal/mol *E*-isomer favored	this work
	- 3.2 kcal/mol	- 2.6 kcal/mol *E*-isomer favored	for comparison ref. 22b

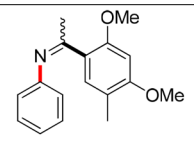
Table 5. Reaction Scope with Various Arenes[a]



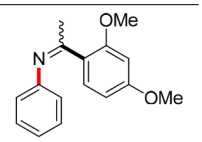
5a - 5h



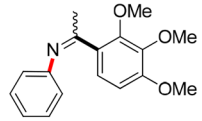
5a R^1 = *p*-*t*-Bu (40%), (*E*/*Z* = 100:0)
5b R^1 = 3,5-diMe (32%), (*E*/*Z* = 100:0)
5c R^1 = 2,4,6-triMe (46%), (*E*/*Z* = 100:0)



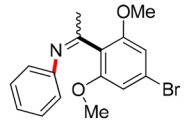
5d (86%), (*Z*/*E* = 80:20)



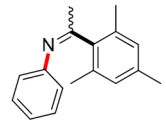
5e (83%), (*Z*/*E* = 76:24)



5f (86%), (*Z*/*E* = 83:17)



5g (78%), (*Z*/*E* = 72:28)



5h (33%), (*Z*/*E* = 50:50)

[a]Reaction conditions: diazonium salt (0.52 mmol) and 1,3,5-$C_6H_3(OMe)_3$ (0.57 mmol) in RCN (2 mL) were heated to 80 °C for 2h; *E*/*Z* ratios determined by ^{1}H NMR.

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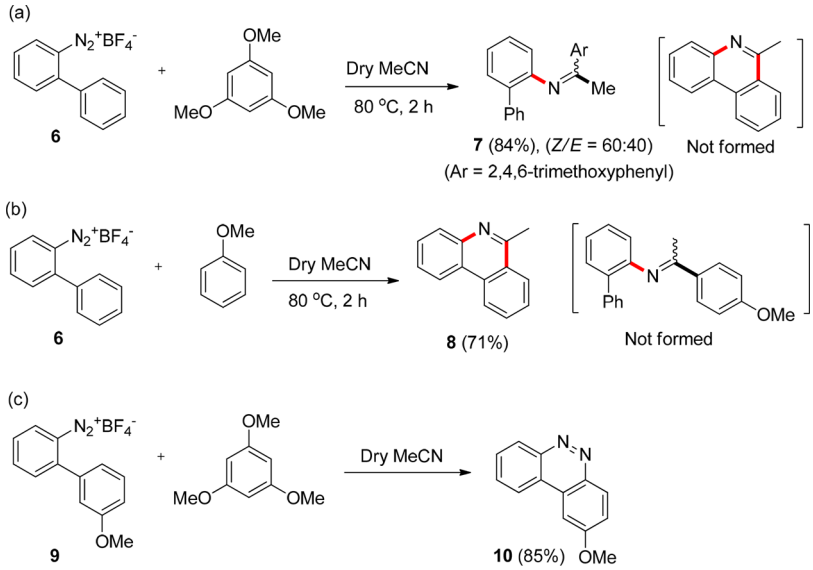
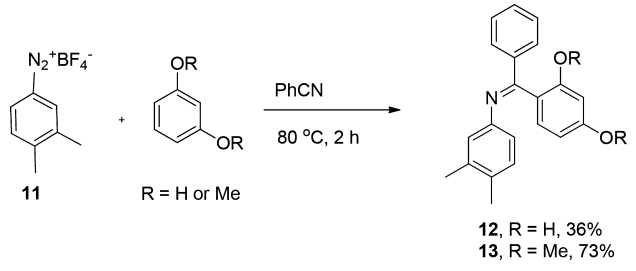
Scheme 3



much faster than that of the intramolecular pathway presumably due to the higher reactivity of the electron-rich arene component. On the other hand, when the less reactive anisole was employed, 6-methylphenanthridine (**8**) was formed in 71% yield via an intramolecular cyclization of the *N*-arylnitrilium intermediate (Scheme 3b).[19a] Interestingly, aryldiazonium salt **9** with an electron-rich *o*-phenyl moiety furnished 2-methoxybenzo[*c*]cinnoline **10** in 85% yield as the result of direct diazo coupling (Scheme 3c).[19a]

To demonstrate the preparative utility of this method, a gram scale synthesis of **4f** was performed under the standard conditions. Typically, the reaction of **1a** (1.0 g) with 1,3,5-trimethoxybenzene (0.97g) in benzonitrile (20 mL) delivered **4f** with complete *Z* selectivity (1.4 g, 78%) (**Caution:** *Aryldiazonium tetrafluoroborates are explosive upon heating, and reactions must be performed using precautions such as protective shielding equipment*). To further showcase the synthetic utility, we also attempted the synthesis of **12** which is known to be a potential fungicide.[23] To our delight, treatment of 3,4-dimethylphenyl diazonium salt **11** with resorcinol in benzonitrile under the optimized conditions provided **12** in acceptable yields with complete *Z* selectivity (Scheme 4). In another run,

Scheme 4. Synthesis of Fungicidal Compounds



we found that **1a** reacted with resorcinol in acetonitrile with 62% of product formation, but it decomposed during the chromatographic purification and afforded only a 36% yield. On the other hand, a gram scale synthesis of dimethoxy analogue **13** was achieved in 73% yield, thus demonstrating the applicability of our method for gram scales via a transition-metal-free approach.

In summary, we have disclosed a transition-metal-free and one-pot strategy to construct diversely substituted *N*-arylketimines from the reaction of aryldiazonium salts, activated arenes, and nitriles. A broad range of substituents and typical functional groups are tolerated, and the corresponding *N*-arylketimines were isolated in high yields even in gram scale reactions. This convenient approach represents mild reaction conditions, atom-efficient, and experimental simplicity, demonstrating feasibility for industrial applications.

EXPERIMENTAL SECTION

General Information. ^{1}H and ^{13}C NMR were recorded in a 400 MH_Z spectrometer in $CDCl_3$ and CD_3CN referenced to TMS. All the nitriles were dried over activated 4Å molecular sieves, and solid nitriles were purchased and used without any further drying. All the anilines were commercially purchased and used for diazotization without further purification. Other chemicals were used as purchased. Flash chromatography was performed using silica gel 230−400 mesh. Aryldiazonium salts were prepared according to the literature procedure. In cases of known compounds, their ^{1}H and ^{13}C NMR values were compared with the literature values. For NMR data, only major product peaks are listed. Melting points were determined on a Fargo MP-1D instrument. Unless otherwise noted, all the reactions were performed without any special precautions.

General Procedure for Preparing Aryldiazonium Tetrafluoroborate. All the substituted aryldiazonium salts were synthesized by following the reported methods. Spectral data of the compounds are in agreement with those reported in the literature. A typical procedure for preparing benzenediazonium tetrafluoroborate is shown below.[19] The corresponding aniline (0.93 g, 10 mmol) was dissolved in a mixture of water (4 mL) and 50% aqueous hydrofluoroboric acid (3.3 mL, 19.3 mmol, 1.92 equiv). The mixture was cooled to 0 °C, and a solution of $NaNO_2$ (0.69 g,10 mmol in 1.5 mL of water) was added slowly. The resulting reaction mixture was stirred at 0 °C for 30 min, and the precipitate was collected by filtration. The solid product was dissolved in minimum acetone and reprecipitated using diethyl ether to yield aryldiazonium tetrafluoroborate which was dried under vacuum without further purification.

General Procedure for the Synthesis of *N*-Arylketimines. In a dry 10 mL glass sealed tube, aryldiazonium salt (100 mg, 0.52 mmol) and 1,3,5-trimethoxybenzene (96 mg, 0.57 mmol, 1.1 equiv) were suspended in 2 mL of anhydrous nitrile. The tube was sealed with a Teflon screw cap and heated in an oil bath (80 °C) for 2 h. After cooling to room temperature, the reaction mixture was diluted with

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DCM (20 mL) and washed with saturated aq. $NaHCO_3$ solution (5 mL). The organic layer was dried over anhydrous Na_2SO_4. Solvents were removed, and the product was purified by column chromatography (eluent: 2% to 20% EtOAc:hexane with 1% Et_3N) to obtain the title compound.

*(E)-1-(4-Methoxyphenyl)-N-phenylethan-1-imine (**2**).*[24] 47 mg, 41%, white solid; *E*/*Z* (100:0); mp 86−87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 11.6, 2.8 Hz, 2H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.94 (dd, *J* = 11.6, 2.8 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 2H), 3.85 (s, 3H), 2.18 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.5, 161.5, 151.7, 132.1, 128.9, 128.8, 122.9, 119.5, 113.5, 55.3, 17.1; HRMS (ESI-TOF) calcd for $C_{15}H_{16}NO$ $(M + H)^+$ *m*/*z* = 226.1232, found 226.1229.

*(Z)-N-Phenyl-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3a**).* 128 mg, 87%, colorless oil; *Z*/*E* (84:16); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.0 Hz, 2H), 6.84 (t, *J* = 7.2 Hz, 1H), 6.67 (d, *J* = 7.2 Hz, 2H), 5.90 (s, 2H), 3.69 (s, 3H), 3.64 (s, 6H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.3, 161.4, 156.5, 151.3, 127.6, 122.9, 119.5, 109.6, 89.9, 55.2, 55.1, 28.0; HRMS (ESI-TOF) calcd for $C_{17}H_{20}NO_3$ $(M + H)^+$ *m*/*z* = 286.1443, found 286.1450.

*(Z)-N-(p-Tolyl)-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3b**).* 133 mg, 92%, colorless oil; *Z*/*E* (83:17); *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 8.4 Hz, 2H), 5.91 (s, 2H), 3.69 (s, 3H), 3.64 (s, 6H), 2.34 (s, 3H), 2.15 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7, 161.2, 156.6, 149.0, 132.2, 128.7, 119.3, 109.9, 89.9, 55.3, 55.1, 28.1, 20.75; HRMS (ESI-TOF) calcd for $C_{18}H_{22}NO_3$ $(M + H)^+$ *m*/*z* = 300.1600, found 300.1589.

*(Z)-N-(4-(tert-Butyl)phenyl)-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3c**).* 103 mg, 76%, colorless oil; *Z*/*E* (77:23); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.4 Hz, 2H), 6.57 (d, *J* = 8.4 Hz, 2H), 5.91 (s, 2H), 3.70 (s, 3H), 3.61 (s, 6H), 2.34 (s, 3H), 1.18 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.3, 161.2, 156.7, 148.7, 145.4, 124.3, 119.2, 110.1, 90.0, 55.3, 55.2, 34.0, 31.3, 28.2; HRMS (ESI-TOF) calcd for $C_{21}H_{28}NO_3$ $(M + H)^+$ *m*/*z* = 342.2069, found 342.2062.

*(Z)-N-(4-Chlorophenyl)-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3d**).* 58 mg, 41%, colorless oil; *Z*/*E* (89:11); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01−6.98 (m, 2H), 6.61−6.58 (m, 2H), 5.91 (s, 2H), 3.71 (s, 3H), 3.65 (s, 6H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.3, 161.6, 156.5, 150.0, 128.2, 127.8, 121.0, 109.2, 90.0, 55.3, 55.2, 28.0; HRMS (ESI-TOF) calcd for $C_{17}H_{19}Cl^{35}NO_3$ $(M + H)^+$ *m*/*z* = 320.1053, found 320.1053; HRMS (ESI-TOF) calcd for $C_{17}H_{19}Cl^{37}NO_3$ $(M + H)^+$ *m*/*z* = 322.1023, found 322.1020.

*(Z)-N-(3-Bromophenyl)-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3e**).* 121 mg, 90%, red oil; *Z*/*E* (85:15); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97−6.94 (m, 1H), 6.90−6.85 (m, 2H), 6.56−6.53 (m, 1H), 5.91 (s, 2H), 3.70 (s, 3H), 3.67 (s, 6H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.5, 161.5, 156.4, 153.2, 129.0, 125.6, 122.7, 121.1, 118.0, 109.3, 89.9, 55.3, 55.2, 28.0; HRMS (ESI-TOF) calcdfor $C_{17}H_{19}{}^{79}BrNO_3$ $(M + H)^+$ *m*/*z* = 364.0548, found 364.0544; HRMS (ESI-TOF) calcd for $C_{17}H_{19}{}^{81}BrNO_3$ $(M + H)^+$*m*/*z* = 366.0528, found 366.0508.

*(Z)-N-(3-Methoxyphenyl)-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3f**).* 121 mg, 92%, colorless oil; *Z*/*E* (83:17); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89−6.85 (m, 1H), 6.40−6.32 (m, 1H), 6.21−6.20 (m, 2H), 5.84 (s, 2H), 3.62 (s, 3H), 3.59 (s, 6H), 3.56 (s, 3H), 2.28 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.0, 161.3, 159.1, 156.4, 152.9, 128.3, 111.9, 109.8, 109.0, 104.7, 89.9, 55.2, 55.1, 54.8, 28.0; HRMS (ESI-TOF) calcd for $C_{18}H_{22}NO_4$ $(M + H)^+$*m*/*z* = 316.1549, found 316.1548.

*(Z)-N-(2-(Methylthio)phenyl)-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3g**).* 103 mg, 74%, colorless oil; *Z*/*E* (73:27); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12−7.01 (m, 2H), 6.87 (td, *J* = 15.0, 1.2 Hz, 1H), 6.72 (td, *J* = 15.0, 1.2 Hz, 1H), 5.91 (s, 2H), 3.70 (s, 3H), 3.61 (s, 6H), 2.43 (s, 3H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.8, 161.3, 157.1, 148.3, 131.2, 125.9, 125.2, 124.3, 123.7, 109.4, 89.9, 55.1, 55.9, 28.0, 15.5; HRMS (ESI-TOF) calcd for $C_{18}H_{22}NO_3S$-$(M + H)^+$ *m*/*z* = 332.1320, found 332.1315.

*(Z)-Ethyl 4-((1-(2,4,6-Trimethoxyphenyl)ethylidene)amino)-benzoate (**3h**).* 105 mg, 78%, colorless oil; *Z*/*E* (89:11); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 5.87 (s, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.68 (s, 3H), 3.64 (s, 6H), 2.35 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.8, 166.7, 161.5, 156.4, 156.1, 129.5, 124.8, 119.2, 109.2, 89.8, 60.4, 55.2, 55.1, 28.0, 14.2; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NO_5$ $(M + H)^+$ *m*/*z* = 358.1654, found 358.1666.

*(Z)-Phenyl (4-((1-(2,4,6-Trimethoxyphenyl)ethylidene)amino)-phenyl)methanone (**3i**).* 116 mg, 88%, colorless oil; *Z*/*E* (88:12); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.64 (m, 2H), 7.58−7.56 (m, 2H), 7.51−7.47 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.89 (s, 2H), 3.69 (s, 3H), 3.65 (s, 6H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.1, 167.3, 161.8, 156.4, 155.8, 138.2, 132.0, 131.7, 130.6, 129.6, 128.0, 119.2, 109.1, 89.9, 55.2, 55.1, 28.0; HRMS (ESI-TOF) calcd for $C_{24}H_{24}NO_4$ $(M + H)^+$ *m*/*z* = 390.1705, found 390.1720.

*(Z)-N-(3,5-Dimethylphenyl)-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3k**).* 116 mg, 82%, colorless oil; *Z*/*E* (75:25); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (s, 1H), 6.28 (s, 2H), 5.90 (s, 2H), 3.69 (s, 3H), 3.65 (s, 6H), 2.33 (s, 3H), 2.11 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.5, 161.1, 156.5, 151.7, 136.8, 124.3, 117.0, 110.1, 89.9, 55.2, 55.1, 28.0, 21.2, 21.1; HRMS (ESI-TOF) calcd for $C_{19}H_{24}NO_3$ $(M + H)^+$ *m*/*z* = 314.1756, found 314.1762.

*(Z)-N-Mesityl-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**3l**).* 82 mg, 59%, colorless oil; *Z*/*E* (96:4); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 2H), 6.15 (s, 2H), 3.81 (s, 3H), 3.79 (s, 6H), 2.11 (s, 6H), 1.83 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.3, 161.0, 157.9, 146.1, 131.5, 128.2, 125.9, 113.8, 90.7, 55.5, 55.3, 21.7, 20.6, 17.6; HRMS (ESI-TOF) calcd for $C_{20}H_{26}NO_3$ $(M + H)^+$ *m*/*z* = 328.1913, found 328.1912.

*(Z)-1-(2,4,6-Trimethoxyphenyl)-N-(3,4,5-trimethoxyphenyl)-ethan-1-imine (**3m**).* 115 mg, 86%, colorless oil; *Z*/*E* (91:9); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (s, 2H), 5.91 (s, 2H), 3.70 (s, 3H), 3.69 (s, 3H), 3.64 (s, 6H), 3.62 (s, 6H), 2.32 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.7, 161.4, 156.4, 152.3, 147.3, 133.6, 109.7, 97.0, 89.9, 60.7, 55.6, 55.3, 55.2, 28.0; HRMS (ESI-TOF) calcd for $C_{20}H_{26}NO_6$ $(M + H)^+$ *m*/*z* = 376.1760, found 376.1763.

*(Z)-3-Methyl-7-((1-(2,4,6-trimethoxyphenyl)ethylidene)amino)-2H-chromen-2-one (**3n**).* 85 mg, 64%, colorless oil; *Z*/*E* (90:10); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.4 Hz, 1H), 6.67 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.60 (d, *J* = 1.6 Hz, 1H), 6.06 (s, 1H), 5.89 (s, 2H), 3.69 (s, 3H), 3.68 (s, 6H), 2.37 (s, 3H), 2.29 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.1, 161.7, 161.4, 156.3, 155.1, 153.6, 152.5, 123.9, 116.7, 115.4, 112.6, 108.8, 107.1, 89.9, 55.3, 55.1, 28.0, 18.5; HRMS (ESI-TOF) calcd for $C_{21}H_{22}NO_5$ $(M + H)^+$ *m*/*z* = 368.1498, found 368.1488.

*(Z)-N-phenyl-1-(2,4,6-trimethoxyphenyl)butan-1-imine (**4a**).* 130 mg, 80%, pale yellow oil; *Z*/*E* (94:6); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 7.6 Hz, 2H), 6.85−6.80 (m, 1H), 6.67 (dd, *J* = 8.4, 1.2 Hz, 2H), 5.89 (s, 2H), 3.68 (s, 3H), 3.62 (s, 6H), 2.61 (t, *J* = 7.6 Hz, 2H), 1.65 (sext, *J* = 7.6 Hz, 2H), 0.98 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.3, 161.3, 156.8, 151.5, 127.5, 122.7, 119.5, 109.2, 89.8, 55.2, 55.1, 43.0, 19.2, 13.9; HRMS (ESI-TOF) calcd for $C_{19}H_{24}NO_3$ $(M + H)^+$ *m*/*z* = 314.1756, found 314.1768.

*(Z)-2-Methyl-N-phenyl-1-(2,4,6-trimethoxyphenyl)propan-1-imine (**4b**).* 102 mg, 63%, pale yellow oil; *Z*/*E* (100:0); *Z*-isomer: ^{1}H NMR (400 MHz, CDCl3) δ 7.01 (t, *J* = 8.0 Hz, 2H), 6.79 (t, *J* = 7.2 Hz, 1H), 6.62 (d, *J* = 8.0 Hz, 2H), 5.88 (s, 2H), 3.69 (s, 3H), 3.62 (s, 6H), 2.80 (sept, *J* = 6.8 Hz, 1H), 1.18 (d, *J* = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.9, 161.1, 156.9, 152.3, 127.4, 122.4, 119.2, 109.4, 89.8, 55.2, 55.1, 38.3, 19.7; HRMS (ESI-TOF) calcd for $C_{19}H_{24}NO_3$ $(M + H)^+$ *m*/*z* = 314.1756, found 314.1769.

*(Z)-1-Cyclopropyl-N-phenyl-1-(2,4,6-trimethoxyphenyl)-methanimine (**4c**).* 116 mg, 72%, colorless oil; *Z*/*E* (92:8); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03−6.98 (m, 2H), 6.79 (tt, *J* = 7.2, 1.2 Hz, 1H), 6.65−6.62 (m, 2H), 5.87 (s, 2H), 3.67 (s, 3H), 3.65 (s, 6H), 2.02−1.95 (m, 1H), 0.86−0.81 (m, 2H), 0.80−0.75 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.9, 161.3, 157.0, 152.0, 127.5, 122.4, 119.2, 106.7, 89.8, 55.2, 55.0, 20.6, 7.4; HRMS (ESI-TOF) calcd for $C_{19}H_{22}NO_3$ $(M + H)^+$ *m*/*z* = 312.1600, found 312.1598.

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*(Z)-2,2-Dimethyl-N-phenyl-1-(2,4,6-trimethoxyphenyl)propan-1-imine (**4d**).* 126 mg, 74%, pale yellow oil; *Z*/*E* (100:0); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02−6.98 (m, 2H), 6.78 (tt, J = 14.8, 0.8 Hz, 1H), 6.62 (dd, J = 8.4, 1.2 Hz, 2H), 5.87 (s, 2H), 3.67 (s, 3H), 3.65 (s, 6H), 1.21 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.8, 156.5, 152.3, 127.5 (2C), 122.3, 118.4, 108.7, 89.6, 55.0, 40.2, 28.8; HRMS (ESI-TOF) calcd for $C_{20}H_{26}NO_3$ $(M + H)^+$ m/z = 328.1913, found 328.1916.

*(Z)-2-Chloro-N-phenyl-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**4e**).* 137 mg, 83%, pale brown oil; *Z*/*E* (100:0); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (t, J = 8.0 Hz, 2H), 6.88 (t, J = 7.6 Hz, 1H), 6.68 (d, J = 7.6 Hz, 2H), 5.91 (s, 2H), 4.48 (s, 2H), 3.69 (s, 3H), 3.61 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.2, 162.0, 157.6, 150.5, 127.6, 123.5, 119.4, 105.4, 90.0, 55.3, 55.1, 48.4; HRMS (ESI-TOF) calcd for $C_{17}H_{19}{}^{35}ClNO_3$ $(M + H)^+$ m/z = 320.1053, found 320.1059; HRMS (ESI-TOF) calcd for $C_{17}H_{19}{}^{37}ClNO_3$ $(M + H)^+$ m/z = 322.1023, found 322.1012.

*(Z)-N,1-Diphenyl-1-(2,4,6-trimethoxyphenyl)methanimine (**4f**).* 151 mg, 82%, off-white solid; mp 118−119 °C; *Z*/*E* (100:0); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.2 Hz, 2H), 7.41−7.33 (m, 3H), 7.11 (t, J = 7.6 Hz, 2H), 6.89 (t, J = 7.2 Hz, 1H), 6.78 (d, J = 7.6 Hz, 2H), 5.98 (s, 2H), 3.74 (s, 3H), 3.57 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.2, 161.7, 157.7, 152.2, 139.3, 130.1, 128.0, 127.9, 127.6, 122.9, 119.1, 107.2, 90.0, 55.3, 55.1; HRMS (ESI-TOF) calcd for $C_{22}H_{22}NO_3$ $(M + H)^+$ m/z = 348.1600, found 348.1609.

*(Z)-N-Phenyl-1-(o-tolyl)-1-(2,4,6-trimethoxyphenyl)methanimine (**4g**).* 113 mg, 61%, off-white solid; mp 140−141 °C; *Z*/*E* (100:0); *Z*-isomer: ^{1}H NMR (400 MHz, CDCl3) δ 7.28 (d, J = 7.6 Hz, 1H), 7.23−7.18 (m, 2H), 7.14−7.08 (m, 3H), 6.89 (t, J = 7.2 Hz, 1H), 6.79 (d, J = 7.6 Hz, 2H), 5.92 (s, 2H), 3.71 (s, 3H), 3.55 (s, 6H), 2.58 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.1, 161.7, 157.5, 152.0, 140.4, 137.1, 130.9, 128.9, 128.4, 127.7, 125.0, 122.9, 119.3, 109.9, 90.1, 55.3, 55.1, 20.4; HRMS (ESI-TOF) calcd for $C_{23}H_{24}NO_3$ $(M + H)^+$ m/z = 362.1756, found 362.1757.

*(Z)-1-(3-Bromophenyl)-N-phenyl-1-(2,4,6-trimethoxyphenyl)-methanimine (**4h**).* 128 mg, 58%, off-white solid; mp 132−133 °C; *Z*/*E* (100:0); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.52−7.49 (m, 1H), 7.20 (t, J = 8.0 Hz, 1H), 7.10 (td, J = 13.8, 2.0 Hz, 2H), 6.90 (t, J = 7.2 Hz, 1H), 6.75 (dd, J = 8.4, 1.2 Hz, 2H), 5.96 (s, 2H), 3.74 (s, 3H), 3.57 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.1, 157.8, 121.6, 141.4, 133.0, 130.8, 129.6, 127.8, 126.7, 123.3, 122.5, 119.1, 106.4, 90.1, 55.4, 55.2; HRMS (ESI-TOF) calcd for $C_{22}H_{21}{}^{79}BrNO_3$ $(M + H)^+$ m/z = 426.0705, found 426.0699; HRMS (ESI-TOF) calcdfor $C_{22}H_{21}{}^{81}BrNO_3$ $(M + H)^+$ m/z = 428.0685, found 428.0636.

*(E)-N-(4-(tert-Butyl)phenyl)-1-(4-methoxyphenyl)ethan-1-imine (**5a**).* 47 mg, 40%, white solid; mp 116−117 °C; *E*/*Z* (100:0); *E*-isomer: ^{1}H NMR (400 MHz, CDCl3) δ 7.95 (d, J = 8.8 Hz, 2H), 7.34 (dd, J = 6.8, 2.0 Hz, 2H), 6.93 (dd, J = 7.2, 2.0 Hz, 2H), 6.73 (d, J = 8.4 Hz, 2H), 3.84 (s, 3H), 2.21 (s, 3H), 1.31 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.9, 161.6, 148.3, 146.0, 131.9, 128.9, 125.6, 119.5, 113.6, 55.3, 34.2, 31.4, 17.2; HRMS (ESI-TOF) calcd for $C_{19}H_{24}NO$ $(M + H)^+$ m/z = 282.1858, found 282.1867.

*(E)-N-(3,5-Dimethylphenyl)-1-(4-methoxyphenyl)ethan-1-imine (**5b**).*[25] 36 mg, 32%, colorless oil; *E*/*Z* (100:0); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 6.70 (s, 1H), 6.40 (s, 2H), 3.84 (s, 3H), 2.28 (s, 6H), 2.19 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.5, 138.5, 132.0, 130.5, 128.8, 124.8, 117.3, 113.5(2C), 55.3, 21.3, 17.2; HRMS (ESI-TOF) calcd for $C_{17}H_{20}NO$ $(M + H)^+$ m/z = 254.1545, found 254.1547.

*(E)-N-Mesityl-1-(4-methoxyphenyl)ethan-1-imine (**5c**).*[26] 46 mg, 53%, colorless oil; *E*/*Z* (100:0); *E*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00−7.97 (m, 2H), 6.98−6.94 (m, 2H), 6.86 (s, 2H), 3.86 (s, 3H), 2.27 (s, 3H), 2.02 (s, 3H), 1.98 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.4, 161.4, 146.4, 131.9, 131.6, 128.6, 128.4, 125.7, 113.5, 55.3, 20.6, 17.8, 17.1; HRMS (ESI-TOF) calcd for $C_{18}H_{22}NO$ $(M + H)^+$ m/z = 268.1701, found 268.1710.

*(Z)-1-(2,4-Dimethoxy-5-methylphenyl)-N-phenylethan-1-imine (**5d**).* 121 mg, 86%, colorless oil; *Z*/*E* (80:20); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.32 (t, J = 7.6 Hz, 2H), 7.04 (t, J = 7.2 Hz, 1H), 6.82 (dd, J = 8.4, 0.8 Hz, 2H), 6.43 (s, 1H), 3.85 (s, 6H), 2.18 (s, 3H), 2.17 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.2, 159.7, 157.1, 151.4, 131.3, 128.7, 122.8, 122.5, 119.5, 118.5, 94.9, 55.7, 55.3, 21.0, 15.0; HRMS (ESI-TOF) calcd for $C_{17}H_{20}NO_2$ $(M + H)^+$ m/z = 270.1494, found 270.1506.

*(Z)-1-(2,4-Dimethoxyphenyl)-N-phenylethan-1-imine (**5e**).* 112 mg, 83%, colorless oil; *Z*/*E* (76:24); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.4 Hz, 1H), 7.34−7.29 (m, 2H), 7.05−7.02 (m, 1H), 6.82−6.80 (m, 2H), 6.53 (dd, J = 8.4, 2.0 Hz, 1H), 6.48 (d, J = 2.4 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 2.16 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.1, 162.0, 158.8, 151.4, 130.7, 128.7, 128.0, 122.9, 119.5, 104.6, 98.6, 55.3, 55.1, 21.0; HRMS (ESI-TOF) calcd for $C_{16}H_{18}NO_2$ $(M + H)^+$ m/z = 256.1338, found 256.1348.

*(Z)-N-Phenyl-1-(2,3,4-trimethoxyphenyl)ethan-1-imine (**5f**).* 129 mg, 86%, colorless oil; *Z*/*E* (83:17); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.30 (m, 3H), 7.09−7.05 (m, 1H), 6.80 (d, J = 7.2 Hz, 2H), 6.70 (d, J = 8.8 Hz, 1H), 3.93 (s, 3H), 3.86 (s, 6H), 2.17 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.7, 154.8, 152.2, 151.1, 142.0, 128.8, 128.1, 123.8, 123.1, 119.3, 107.2, 61.3, 60.8, 56.0, 20.8; HRMS (ESI-TOF) calcd for $C_{17}H_{20}NO_3$ $(M + H)^+$ m/z = 286.1443, found 286.1449.

*(Z)-1-(4-Bromo-2,6-dimethoxyphenyl)-N-phenylethan-1-imine (**5g**).* 135 mg, 78%, yellow oil; *Z*/*E* (72:28); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09−7.05 (m, 2H), 6.90−6.87 (m, 1H), 6.78 (dd, J = 8.4, 0.8 Hz, 2H), 6.48 (d, J = 2.0 Hz, 1H), 6.20 (d, J = 2.0 Hz, 1H), 3.69 (s, 3H), 3.65 (s, 3H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.2, 160.5, 156.8, 150.5, 127.8, 123.3, 119.2, 108.2, 97.4, 55.4, 55.3, 27.4; HRMS (ESI-TOF) calcd for $C_{16}H_{17}{}^{79}BrNO_2$ $(M + H)^+$ m/z = 334.0443, found 334.0439; HRMS (ESI-TOF) calcd for $C_{17}H_{19}{}^{81}BrNO_3$ $(M + H)^+$ m/z = 336.0423, found 336.0405.

*(Z)-1-Mesityl-N-phenylethan-1-imine (**5h**).* 41 mg, 33%, colorless oil; *Z*/*E* (50:50); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.35 (m, 1H), 7.10−7.08 (m, 2H), 6.86−6.84 (m, 2H), 6.69 (s, 2H), 2.37 (s, 3H), 2.32 (s, 6H), 2.16 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.0, 150.1, 137.2 (2C), 132.8, 128.4, 128.0, 123.6, 119.9, 28.6, 20.9, 19.8; *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.30 (m, 1H), 7.07−7.05 (m, 1H), 6.91−6.87 (m, 3H), 6.67 (s, 2H), 2.27 (s, 3H), 2.15 (s, 6H), 2.04 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.5, 150.9, 138.8, 136.0, 133.3, 129.0, 128.1, 123.4, 119.2, 21.4, 21.0, 19.0; HRMS (ESI-TOF) calcd for $C_{17}H_{20}N$ $(M + H)^+$ m/z = 238.1596, found 238.1594.

*(Z)-N-([1,1′-Biphenyl]-2-yl)-1-(2,4,6-trimethoxyphenyl)ethan-1-imine (**7**).* 113 mg, 84%, colorless oil; *Z*/*E* (60:40); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.2 Hz, 2H), 7.35 (d, J = 7.8 Hz, 1H), 7.32−7.29 (m, 2H), 7.28−7.25 (m, 1H), 6.99−6.94 (m, 2H), 6.61−6.59 (m, 1H), 5.92 (s, 2H), 3.72 (s, 3H), 3.51 (s, 6H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.6, 161.3, 157.1, 147.9, 140.1, 133.0, 129.8, 129.6, 127.5, 127.4, 126.2, 123.7, 119.7, 109.7, 89.9, 55.6, 55.0, 28.1; *E*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.45 (m, 2H), 7.39−7.38 (m, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.28−7.26 (m, 2H), 7.25−7.23 (m, 1H), 7.16−7.12 (m, 1H), 6.87 (dd, J = 7.6, 1.04 Hz, 1H), 6.08 (s, 2H), 3.77 (s, 3H), 3.68 (s, 6H), 1.92 (s, 3H); HRMS (ESI-TOF) calcd for $C_{23}H_{24}NO_3$ $(M + H)^+$ m/z = 362.1756, found 362.1767.

*6-Methylphenanthridine (**8**).*[19a] 51 mg, 71%, viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 8.4, 0.4 Hz, 1H), 8.50 (dd, J = 8.4, 1.6 Hz, 1H), 8.20−8.17 (m, 1H), 8.09 (dd, J = 8.0, 0.8 Hz, 1H), 7.81 (td, J = 7.6, 1.6 Hz, 1H), 7.71−7.64 (m, 2H), 7.59 (td, J = 7.6, 1.2 Hz, 1H), 3.02 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.8, 143.6, 132.5, 130.4, 129.2, 128.6, 127.2, 126.5, 126.3, 125.8, 123.7, 122.2, 121.9, 23.3. HRMS(ESI) calcd for $C_{14}H_{12}N$ $(M + 1)^+$ m/z = 194.0970, found: 194.0976.

*2-Methoxybenzo[c]cinnoline (**10**).*[19a] 47 mg, 85%, viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68−8.66 (m, 1H), 8.62 (d, J = 9.2 Hz, 1H), 8.50−8.47 (m, 1H), 7.89−7.83 (m, 2H), 7.79 (d, J = 2.4 Hz, 1H), 7.47 (dd, J = 8.8, 2.4 Hz, 1H), 4.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 145.1, 142.0, 133.2, 131.1, 130.7, 129.2, 123.1, 121.4, 120.9, 120.2, 100.5, 55.8. HRMS (ESI) calcd for $C_{13}H_{11}N_2O$ $(M + 1)^+$ m/z = 211.0871, found; 211.0867.

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*(Z)-4-(((3,4-Dimethylphenyl)imino)(phenyl)methyl)benzene-1,3-diol (**12**).*[23] 44 mg, 36%, yellow solid; mp 190−191 °C; *Z*/*E* (100:0): *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.31 (m, 3H), 7.22 (dd, *J* = 7.6, 1.2 Hz, 2H), 6.88 (s, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.78−6.75 (d, *J* = 8.8 Hz, 2H), 6.50 (dd, *J* = 8.4 Hz, 1H), 6.16 (dd, *J* = 8.8, 2.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.3, 169.0, 164.2, 139.2, 137.1, 134.8, 134.2, 132.8, 129.6, 129.4, 129.0, 128.3, 125.0, 120.8, 111.4, 108.1, 104.4; HRMS (ESI-TOF) calcd for $C_{21}H_{20}NO_2$ $(M + H)^+$ *m*/*z* = 318.1494, found 318.1490.

*(Z)-1-(2,4-Dimethoxyphenyl)-N-(3,4-dimethylphenyl)-1-phenylmethanimine (**13**).* 793 mg, 73%, viscous oil; *Z*/*E* (100:0); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 2H), 7.42−7.34 (m, 3H), 6.86 (t, *J* = 15.6 Hz, 2H), 6.64 (s, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 6.38−6.37 (m, 2H), 3.75 (s, 3H), 3.55 (s, 3H), 2.13 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.2, 160.9, 157.8, 149.3, 139.8, 135.8, 130.8, 130.4, 130.0, 129.1, 128.2, 127.9, 121.8, 118.7, 117.1, 104.0, 98.2, 55.07, 55.04, 19.6, 18.9; HRMS (ESI-TOF) calcd for $C_{23}H_{24}NO_2$ $(M + H)^+$ *m*/*z* = 346.1807, found 346.1812.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b01000.

Crystal data for **4f**, bond distances and angles of **4f**, spectra for all new compounds, and computational details (PDF)

Crystallographic data for **4f** (CCDC 1833801) (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Barluenga, J.; Cuervo, H.; Olano, B.; Fustero, S.; Gotor, V. Synthesis of *N*-Aryl-substituted 2-Aminoalkyl Ketones and 1,3-Alkanediamines. *Synthesis* **1986**, *1986*, 469−473. (b) Guijarro, D.; Yus, M. Naphthalene-catalysed Lithiation of Phenone imines in the Presence of Carbonyl Compounds: Preparation of 1,2-Aminoalcohols. *Tetrahedron* **1993**, *49*, 7761−7768. (c) Shibata, I.; Kawakami, T. M.; Tanizawa, D.; Suwa, T.; Sugiyama, E.; Matsuda, H.; Baba, A. Chemoselective Reductions of Imino Groups by Dibutyltin Chloride Hydride Complex. *J. Org. Chem.* **1998**, *63*, 383−385. (d) Tsukinoki, T.; Mitoma, Y.; Nagashima, S.; Kawaji, T.; Hashimoto, I.; Tashiro, M. Organic Reaction in Water. Part 1. A Convenient Method for Reduction of Imines Using Zinc Powder. *Tetrahedron Lett.* **1998**, *39*, 8873−8876. (e) Fustero, S.; de la Torre, M. G.; Jofre, V.; Carlon, R. P.; Navarro, A.; Fuentes, A. S. Synthesis and Reactivity of New β-Enamino Acid Derivatives: A Simple and General Approach to β-Enamino Esters and Thioesters. *J. Org. Chem.* **1998**, *63*, 8825−8836. (f) Kobayashi, S.; Ishitani, H. Catalytic Enantioselective Addition to Imines. *Chem. Rev.* **1999**, *99*, 1069−1094. (g) Adams, J. P. Imines, Enamines and Oximes. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 125−139. (h) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. Asymmetric Enamine Catalysis. *Chem. Rev.* **2007**, *107*, 5471−5569.

(2) (a) Steinig, A. G.; Spero, D. M. Amines *via* Nucleophilic 1,2-Addition to Ketimines: Construction of Nitrogen Substituted Quaternary Carbon Atoms. A review. *Org. Prep. Proced. Int.* **2000**, *32*, 205−234. (b) Ellman, J. A.; Owens, T. D.; Tang, T. P. *N-tert*-Butanesulfinyl Imines: Versatile Intermediates for the Asymmetric Synthesis of Amines. *Acc. Chem. Res.* **2002**, *35*, 984−995. (c) Wu, Y.; Hu, L.; Li, Z.; Deng, L. Catalytic Asymmetric Umpolung Reactions of Imines. *Nature* **2015**, *523*, 445−450. (d) Rong, J.; Collados, J. F.; Ortiz, P.; Jumde, R. P.; Otten, E.; Harutyunyan, S. R. Catalytic Enantioselective Addition of Grignard Reagents to Aromatic Silyl Ketimines. *Nat. Commun.* **2016**, *7*, 13780−13786.

(3) (a) Cabello, N.; Kizirian, J. C.; Alexakis, A. Enantioselective Addition of Aryllithium Reagents to Aromatic Imines Mediated by 1,2-Diamine Ligands. *Tetrahedron Lett.* **2004**, *45*, 4639−4642. (b) Cabello, N.; Kizirian, J. C.; Gille, S.; Alexakis, A.; Bernardinelli, G.; Pinchard, L.; Caille, J. C. Simple 1,2-Diamine Ligands for Asymmetric Addition of Aryllithium Reagents to Imines. *Eur. J. Org. Chem.* **2005**, *2005*, 4835−4842. (c) Liu, X.; Gao, A.; Ding, L.; Xu, J.; Zhao, B. Aminative Umpolung Synthesis of Aryl Vicinal Diamines from Aromatic Aldehydes. *Org. Lett.* **2014**, *16*, 2118−2121.

(4) (a) Bloch, R. Additions of Organometallic Reagents to C = N Bonds: Reactivity and Selectivity. *Chem. Rev.* **1998**, *98*, 1407−1438. (b) Reddy, L. T.; Gupta, A. P.; Liu, Y. Asymmetric Synthesis of α-Amino Acids by Reduction of *N-tert*-Butanesulfinyl Ketimine Esters. *J. Org. Chem.* **2011**, *76*, 3409−3415. (c) Mita, T.; Chen, J.; Sugawara, M.; Sato, Y. One-Pot Synthesis of α-Amino Acids from Imines through CO2 Incorporation: An Alternative Method for Strecker Synthesis. *Angew. Chem., Int. Ed.* **2011**, *50*, 1393−1396. (d) Yang, K. S.; Rawal, V. H. Synthesis of α-Amino Acid Derivatives and Peptides via Enantioselective Addition of Masked Acyl Cyanides to Imines. *J. Am. Chem. Soc.* **2014**, *136*, 16148−16151.

(5) (a) Wei, Y.; Deb, I.; Yoshikai, N. Palladium-Catalyzed Aerobic Oxidative Cyclization of *N*-Aryl Imines: Indole Synthesis from Anilines and Ketones. *J. Am. Chem. Soc.* **2012**, *134*, 9098−9101. (b) Chen, T.; Chen, X.; Wei, J.; Lin, D.; Xie, Y.; Zeng, W. Copper-Catalyzed Cascade Cycloamination of α-Csp3−H Bond of N-Aryl Ketimines with Azides: Access to Quinoxalines. *Org. Lett.* **2016**, *18*, 2078−2081. (c) Wu, L. L.; Xiang, Y.; Yang, D. C.; Guan, Z.; He, Y. H. Biocatalytic asymmetric Mannich reaction of ketimines using wheat germ lipase. *Catal. Sci. Technol.* **2016**, *6*, 3963−3970. (d) Florio, S.; Troisi, L.; Capriati, V. (Heteroarylchloromethyl)lithiums as Darzens Reagents: Synthesis of Heteroarylaziridine. *J. Org. Chem.* **1995**, *60*, 2279−2282. (e) Chen, X.; Xie, Y.; Xiao, X.; Li, G.; Deng, Y.; Jiang, H.; Zeng, W. Rh(III)-Catalyzed Chelation-Assisted Intermolecular Carbenoid Functionalization of α-Imino Csp^3−H Bonds. *Chem. Commun.* **2015**, *51*, 15328−15331. (f) Wu, J.; Zhou, Y.; Wu, T.; Zhou, Y.; Chiang, C. W.; Lei, A. From Ketones, Amines, and Carbon Monoxide to 4-Quinolones: Palladium-Catalyzed Oxidative Carbonylation. *Org. Lett.* **2017**, *19*, 6432−6435. (g) Lian, Y.; Hummel, J. R.; Bergman, R. G.; Ellman, J. A. Facile Synthesis of Unsymmetrical Acridines and Phenazines by a Rh(III)-catalyzed Amination/Cyclization/Aromatization Cascade. *J. Am. Chem. Soc.* **2013**, *135*, 12548−12551. (h) Kuninobu, Y.; Yu, P.; Takai, K. Rhenium-Catalyzed Diastereoselective Synthesis of Aminoindanes via the Insertion of Allenes into a C−H Bond. *Org. Lett.* **2010**, *12*, 4274−4276.

(6) (a) Charette, A. B. *Chiral Amine Synthesis: Methods, Developments and Applications*; Wiley: 2010; Chapter 1. (b) Ortiz, P.; Collados, J. F.; Jumde, R. P.; Otten, E.; Harutyunyan, S. R. Copper-Catalyzed Enantioselective Alkylation of Enolizable Ketimines with Organomagnesium Reagents. *Angew. Chem., Int. Ed.* **2017**, *56*, 3041−3044.

(7) (a) Small, B. L.; Brookhart, M.; Bennett, A. M. A. Highly Active Iron and Cobalt Catalysts for the Polymerization of Ethylene. *J. Am. Chem. Soc.* **1998**, *120*, 4049−4050. (b) Subbaraj, P.; Ramu, A.; Raman, N.; Dharmaraja, J. Novel Mixed Ligand Complexes of Bioactive Schiff Base (E)-4-(Phenyl(phenylimino)methyl)benzene-1,3-diol and 2-Aminophenol/2-Aminobenzoic acid: Synthesis, Spectral Characterization, Antimicrobial and Nuclease Studies. *Spectrochim. Acta, Part A* **2014**, *117*, 65−71.

DOI: 10.1021/acs.joc.8b01000
J. Org. Chem. 2018, 83, 6133−6141

(8) (a) Selva, M.; Tundo, P.; Marques, C. A. A Simple One-Pot Synthesis of Functionalized Ketimines from Ketones and Amine Hydrochloride Salts. *Synth. Commun.* **1995**, *25*, 369−378. (b) Okubo, M.; Uematsu, Y. The Replacement of Electronegative Substituents by an Electron-Transfer Mechanism. The Factors Governing the Reaction of Carbonyl and Imino Compounds with Organomagnesium Reagents. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1121−1126. (c) Amrutham, V.; Mameda, N.; Kodumuri, S.; Chevella, D.; Banothu, R.; Gajula, K. S.; Grigoreva, N. G.; Nama, N. H*β* Catalyzed Condensation Reaction Between Aromatic Ketones and Anilines: To Access Ketimines (Imines). *Catal. Lett.* **2017**, *147*, 2982−2986 and references cited therein.

(9) (a) Furukawa, S.; Ohno, Y.; Shishido, T.; Teramura, K.; Tanaka, T. Selective Amine Oxidation Using Nb2O5 Photocatalyst and O2. *ACS Catal.* **2011**, *1*, 1150−1153. (b) Largeron, M.; Fleury, M. B. A Biologically Inspired Cu^{I}/Topaquinone-Like Co-Catalytic System for the Highly Atom-Economical Aerobic Oxidation of Primary Amines to Imines. *Angew. Chem., Int. Ed.* **2012**, *51*, 5409−5412. (c) Huang, H.; Huang, J.; Liu, Y. M.; He, H. Y.; Cao, Y.; Fan, K. N. Graphite oxide as an efficient and durable metal-free catalyst for aerobic oxidative coupling of amines to imines. *Green Chem.* **2012**, *14*, 930−934. (d) Wendlandt, A. E.; Stahl, S. S. Chemoselective Organocatalytic Aerobic Oxidation of Primary Amines to Secondary Imines. *Org. Lett.* **2012**, *14*, 2850−2853 and references cited therein.

(10) (a) He, W.; Wang, L.; Sun, C.; Wu, K.; He, S.; Chen, J.; Wu, P.; Yu, Z. Pt−Sn/γ-Al_2O_3-Catalyzed Highly Efficient Direct Synthesis of Secondary and Tertiary Amines and Imines. *Chem. - Eur. J.* **2011**, *17*, 13308−13317. (b) Li, Q.; Fan, S.; Sun, Q.; Tian, H.; Yu, X.; Xu, Q. Copper-catalyzed N-alkylation of amides and amines with alcohols employing the aerobic relay race methodology. *Org. Biomol. Chem.* **2012**, *10*, 2966−2972. (c) Zotova, N.; Roberts, F. J.; Kelsall, G. H.; Jessiman, A. S.; Hellgardt, K.; Hii, K. K. Catalysis in flow: Au-catalysed alkylation of amines by alcohols. *Green Chem.* **2012**, *14*, 226−232. (d) Kang, Q.; Zhang, Y. Copper-catalyzed highly efficient aerobic oxidative synthesis of imines from alcohol and amines. *Green Chem.* **2012**, *14*, 1016−1019 and references cited therein.

(11) (a) Tokunaga, M.; Eckert, M.; Wakatsuki, Y. Ruthenium-Catalyzed Intermolecular Hydroamination of Terminal Alkynes with Anilines: A Practical Synthesis of Aromatic Ketimines. *Angew. Chem., Int. Ed.* **1999**, *38*, 3222−3224. (b) Shanbhag, G. V.; Halligudi, S. B. Intermolecular hydroamination of alkynes catalyzed by zinc-exchanged montmorillonite clay. *J. Mol. Catal. A: Chem.* **2004**, *222*, 223−238. (c) Li, Y.; Shi, Y.; Odom, A. L. Titanium Hydrazido and Imido Complexes: Synthesis, Structure, Reactivity, and Relevance to Alkyne Hydroamination. *J. Am. Chem. Soc.* **2004**, *126*, 1794−1803. (d) Ryken, S. A.; Schafer, L. L. *N,O*-Chelating Four-Membered Metallacyclic Titanium(IV) Complexes for Atom-Economic Catalytic Reactions. *Acc. Chem. Res.* **2015**, *48*, 2576−2586 and reference cited therein.

(12) Song, E.; Kim, H. Y.; Oh, K. Palladium-Catalyzed Aerobic Oxidative Hydroamination of Vinylarenes Using Anilines: A Wacker-Type Amination Pathway. *Org. Lett.* **2017**, *19*, 5264−5267 and reference cited therein.

(13) Sarsah, R. S.; Lutz, M. R., Jr; Bobb, K. C.; Becker, D. P. Metal-free Tandem Beckmann−Electrophilic Aromatic Substitution Cascade Affording Diaryl Imines, Ketones, Amines, and Quinazolines. *Tetrahedron Lett.* **2015**, *56*, 5390−5392.

(14) (a) Morimoto, M.; Sekiya, M. A Convenient Synthetic Method for Schiff Bases. The Trimethylsilyl-Trifluoromethanesulfonate-Catalyzed Reaction of *N,N*-bis(trimethylsilyl)amines with Aldehydes and Ketones. *Chem. Lett.* **1985**, *14*, 1371−1372. (b) Eisch, J. J.; Sanchez, R. Rearrangements of Heterocyclic Compounds. 5. The Selective, Oxophilic Imination of Ketones with Bis(dichloroaluminum)-phenylimide. *J. Org. Chem.* **1986**, *51*, 1848−1852. (c) Okubo, M.; Hayashi, S.; Matsunaga, M.; Uematsu, Y. Iminodimagnesium Reagents. Condensation Reaction with Ketones. Direct Preparation of Anils and a Hydrazone of Xanthone. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2337−2340.

(15) (a) Movassaghi, M.; Hill, M. D. Synthesis of Substituted Pyridine Derivatives via the Ruthenium-Catalyzed Cycloisomerization of 3-Azadienynes. *J. Am. Chem. Soc.* **2006**, *128*, 4592−4593. (b) Huang, P. Q.; Huang, Y. H.; Xiao, K. J. Metal-Free Intermolecular Coupling of Arenes with Secondary Amides: Chemoselective Synthesis of Aromatic Ketimines and Ketones, and *N*-Deacylation of Secondary Amides. *J. Org. Chem.* **2016**, *81*, 9020−9027 and reference cited therein.

(16) (a) Weingarten, H.; Chupp, J. P.; White, W. A. Ketimine Syntheses. Use of Titanium Tetrachloride in a New Procedure for Their Preparation. *J. Org. Chem.* **1967**, *32*, 3246−3249. (b) Moretti, I.; Torre, G. A Convenient Method for the Preparation of *N*-Alkyl Benzophenone Imines. *Synthesis* **1970**, *1970*, 141. (c) Texier-Boullet, F. A Simple, Convenient and Mild Synthesis of Imines on Alumina Surface without Solvent. *Synthesis* **1985**, *1985*, 679−681. (d) Stetin, C.; De Jaso, B.; Pommier, J. C. Imine Synthesis in Strictly Neutral Conditions. *Synth. Commun.* **1982**, *12*, 495−499.

(17) (a) Ghosh, I.; Marzo, L.; Das, A.; Shaikh, R.; Koenig, B. Visible Light Mediated Photoredox Catalytic Arylation Reactions. *Acc. Chem. Res.* **2016**, *49*, 1566−1577. (b) Mo, F.; Dong, G.; Zhang, Y.; Wang, J. Recent Applications of Arene Diazonium Salts in Organic Synthesis. *Org. Biomol. Chem.* **2013**, *11*, 1582−1593. (c) Sun, C. L.; Shi, Z. J. Transition-Metal-Free Coupling Reactions. *Chem. Rev.* **2014**, *114*, 9219−9280. (d) Wang, H.; Xu, Q.; Shen, S.; Yu, S. Synthesis of Quinolines through Three-Component Cascade Annulation of Aryl Diazonium Salts, Nitriles, and Alkynes. *J. Org. Chem.* **2017**, *82*, 770−775 and references therein.

(18) (a) Youn, S. W.; Yoo, H. J.; Lee, E. M.; Lee, S. Y. Metal-Free One-Pot Synthesis of (Tetrahydro)Quinolines through Three-Component Assembly of Arenediazonium Salts, Nitriles, and Styrenes. *Adv. Synth. Catal.* **2018**, *359*, 1−7. (b) van Dijk, T.; Slootweg, J. C.; Lammertsma, K. Nitrilium ions − synthesis and applications. *Org. Biomol. Chem.* **2017**, *15*, 10134−10144 and references therein.

(19) (a) Ramanathan, M.; Liu, S.-T. Preparation of Substituted Phenanthridines from the Coupling of Aryldiazonium Salts with Nitriles: A Metal Free Approach. *J. Org. Chem.* **2015**, *80*, 5329−5336. (b) Ramanathan, M.; Wang, Y. H.; Liu, S.-T. One-Pot Reactions for Synthesis of 2,5-Substituted Tetrazoles from Aryldiazonium Salts and Amidines. *Org. Lett.* **2015**, *17*, 5886−5889. (c) Ramanathan, M.; Liu, S.-T. Preparation of Quinazolines via a 2 + 2+2 Annulation from Aryldiazonium Salts and Nitriles. *J. Org. Chem.* **2017**, *82*, 8290−8295. (d) Ramanathan, M.; Liu, S.-T. Cascade Annulations of Aryldiazonium Salts, Nitriles and Halo-alkynes Leading to 3-Haloquinolines. *Tetrahedron* **2017**, *73*, 4317−4322. (e) Ramanathan, M.; Liu, Y. H.; Peng, S. M.; Liu, S.-T. Synthesis of Substituted Quinazolin-4(3*H*)-imines From Aryldiazonium Salts, Nitriles and 2-Cyanoanilines via A Metal-Free Tandem Approach. *Org. Lett.* **2017**, *19*, 5840−5843.

(20) Moustafa, A. H.; Hitzler, M. G.; Lutz, M.; Jochims, J. C. 3,4-Dihydroquinolinium Salts: Preparation by Reaction of *N*-Arylnitrilium Salts with Alkenes. *Tetrahedron* **1997**, *53*, 625−640.

(21) Wang, M.; Funabiki, K.; Matsui, M. Synthesis and Properties of Bis(hetaryl)azo Dyes. *Dyes Pigm.* **2003**, *57*, 77−86.

(22) (a) van Dijk, T.; Bakker, M. S.; Holtrop, F.; Nieger, M.; Slootweg, J. C.; Lammertsma, K. Base-Stabilized Nitrilium Ions as Convenient Imine Synthons. *Org. Lett.* **2015**, *17*, 1461−1464. (b) Renzi, P.; Hioe, J.; Gschwind, R. M. Decrypting Transition States by Light: Photoisomerization as a Mechanistic Tool in Brønsted Acid Catalysis. *J. Am. Chem. Soc.* **2017**, *139*, 6752−6760.

(23) Giri, S.; Khare, R. K.; Singh, K. K. Synthesis of Some N^{1}-Aryl/Heteroaryl-2,2-Disubstituted Azomethines As Potential Fungicides. *Curr. Sci.* **1981**, *50*, 676−677.

(24) Chelouan, A.; Recio, R.; Borrego, L. G.; Álvarez, E.; Khiar, N.; Fernández, I. Sulfinamide Phosphinates as Chiral Catalysts for the Enantioselective Organocatalytic Reduction of Imines. *Org. Lett.* **2016**, *18*, 3258−3261.

(25) Pham, N. N.; Dang, T. T.; Ngo, N. T.; Villinger, A.; Ehlers, P.; Langer, P. Facile Synthesis of 4- and 7-Azaindoles from the Corresponding Imines by Palladium-Catalyzed Cascade C−C and C−N Coupling. *Org. Biomol. Chem.* **2015**, *13*, 6047−6058.

(26) Kong, L.; Ganguly, R.; Li, Y.; Kinjo, R. Diverse Reactivity of a Tricoordinate Organoboron L_2PhB: (L = oxazol-2-ylidene) Towards Alkali Metal, Group 9 Metal, and Coinage Metal Precursors. *Chem. Sci.* **2015**, *6*, 2893−2902.

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