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Authors: Lou Shi, Ling Pan, Yifei Li, and QUN LIU

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Copper(II)-Catalyzed Aerobic Oxidative Desulfitative 6π Electrocyclization: Efficient Synthesis of Diverse 4-Aminoquinolines

Lou Shi,[a] Ling Pan, [a,b,*] Yifei Li,[a,b] and Qun Liu [a,b,*]

[a] Department of Chemistry, Northeast Normal University, Changchun 130024, China.
Tel (Fax) : +86-(0)431-8509-9759; e-mail: panl948@nenu.edu.cn; liuqun@nenu.edu.cn

[b] Jilin Province Key Laboratory of Organic Functional Molecular Design & Synthesis, Faculty of Chemistry, Northeast Normal University, Changchun 130024, China.

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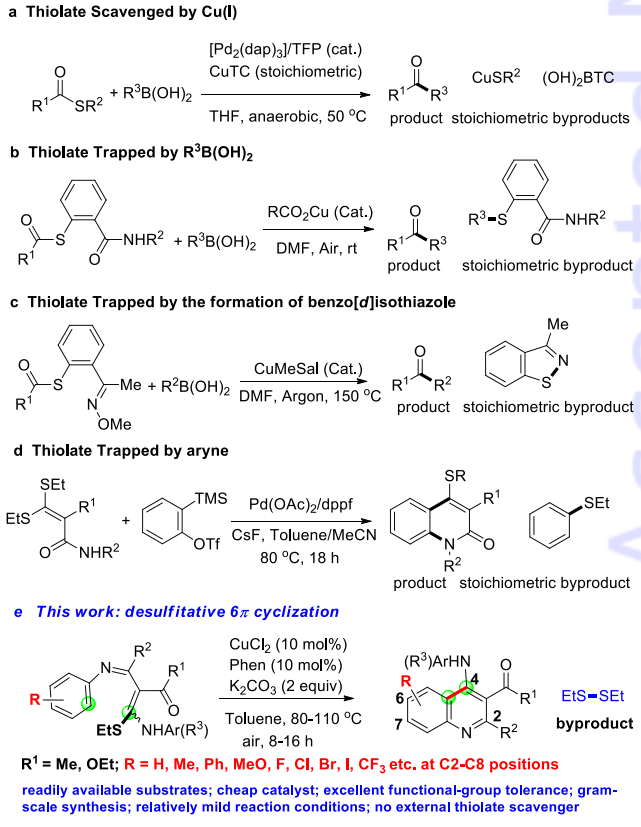
Abstract. The C−C bond formation via C−S bond activation (disclosed in 2000) has received increasing attentions. However, stoichiometric amount of exogenous thiophilic reagents are generally required as thiolate scavengers. Herein, a new model for the synthesis of 4-aminoquinolines, Cu(II)-catalyzed aerobic oxidative desulfitative 6π cyclization of the readily available *N*-aryl-imino ketene *N*,*S*-acetals is described. The reaction can proceed efficiently under mild reaction conditions without any exogenous thiolate scavengers (due to the formation of disulfide as the by-product) to afford diverse 4-aminoquinolines, a privileged structure motif displaying antimalarial activity, with a wide range of functional groups at C2−C8 positions.

Keywords: 6π cyclization; disulfide as by-product; 4-aminoquinolines; heterocycles; imino ketene *N*,*S*-acetals

Introduction

In the rapidly growing area of transition-metal-catalyzed C−C cross-coupling reactions, the C−S bond activation for C−C bond formation,[1] especially as represented by the Liebeskind−Srogl C−C cross-coupling (L−S reaction) and its variants, has received increasing attention and applied in many fields owing to the expansion of both nucleophilic and electrophilic sulfur-containing partners.[1-5] The L−S reaction was disclosed in 2000 aimed at the synthesis of ketones from Pd-catalyzed, Cu(I)-mediated C−C cross-coupling of electrophilic thiol esters with nucleophilic boronic acids under anaerobic, neutral reaction conditions (Scheme 1a).[2a] In this early version, at least a stoichiometric amount of Cu(I) salt, as thiophilic soft Lewis acid, should be used to play both roles as the co-catalyst to activate C−S bond and the scavenger to trap the in-situ generated thiolate.[2a,6] Later on, Cu(I) catalytic systems were studied in details, for example, through modification of thiol ester substrates to achieve efficient catalytic turnover in a thiophilic environment (Scheme 1b and 1c).[2b,c]

Nowadays, although more and more organometallics as nucleophiles and thioorganic compounds as electrophiles have become promising sources for L−S type reactions[1−5] and Cu(II) salt has proven an efficient catalyst under aerobic conditions,[4a] the reaction still faces the challenge using a stoichiometric amount of Cu(I) salt and boronic acid (Scheme 1a),[2a,5] boronic acids (Scheme



Scheme 1. Desulfitative C−C cross-coupling and related reactions.

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1b)[2b,4a] or esters,[3] the special N−O reactant (Scheme 1c),[2c] or arynes (as nucleophilic partners, Scheme 1d)[4b] as thiolate scavenger. In our recent research, the L−S type reaction with ketene *S,S*-acetals[7] as the thioorganic components[4] was succeeded. However, a stoichiometric amount of thiolate scavenger, such as, an arylboronic acid[4a] or an aryne (Scheme 1d),[4b] was still necessary.

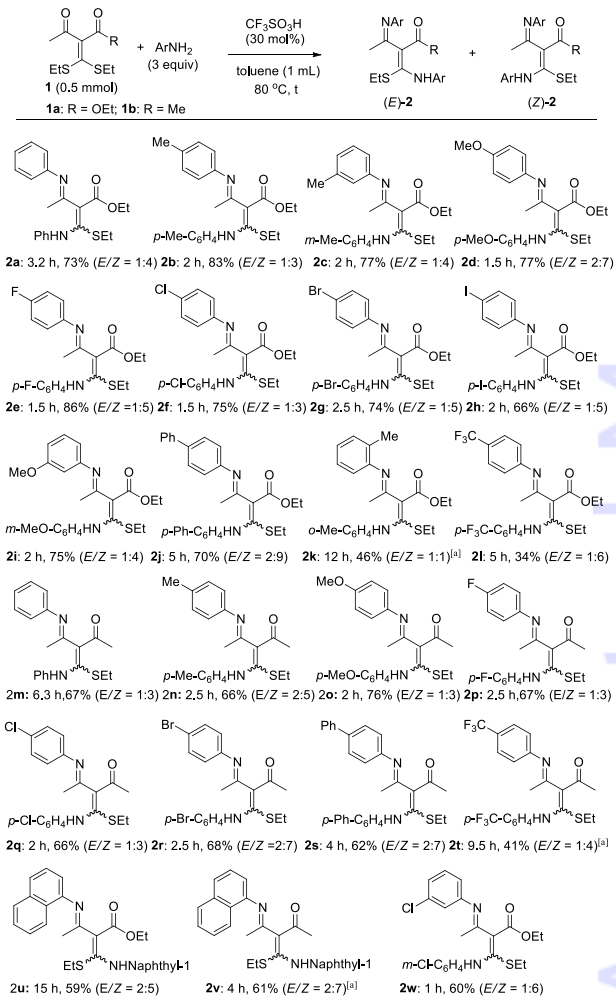
Over the last two decades, transition-metal-catalyzed C−H bond activation for C−C bond formation[8] has rapidly grown into an active area of research for their atom- and step-economical features.[9] Herein, we describe a new reaction model, Cu(II)-catalyzed aerobic oxidative desulfitative 6π cyclization for the construction of 4-aminoquinolines. This reaction can proceed under aerobic conditions to provide an alternative to dual C−H/C−S activation for C−C bond formation process without the requirement of expensive organometallic reagents as thiolate scavengers (Scheme 1e). Based on this new reaction, a simple and practical approach to diverse 4-aminoquinolines, a privileged structure motif displaying antimalarial activity,[10] with a wide range of functional groups at C2−C8 positions, which would otherwise be difficult to synthesize,[10,11] is presented.

Results and Discussion

As our continuing research on the C−S bond activation for C−C bond formation reaction,[4] the intramolecular version of the C−S activation for C−C bond forming reaction was carried out at first using *N*-aryl-imino ketene *N,S*-acetals **2** as the starting materials. For the preparation of **2**, catalyzed by $BF_3{\cdot}Et_2O$ (30 mol%),[12] the model reaction (Table 1) of the readily available ketene *S,S*-acetal **1a** bearing an acetyl and an ethoxyl carbonyl group, respectively, at the terminal carbon[7a] was reacted with aniline (3 equiv) in toluene by adding aniline (toluene solution) in 3 portions to the mixture of **1a** and $BF_3{\cdot}Et_2O$ within 1 h. As the result, ketene *N,S*-acetal **2a**, as an *E*/*Z* mixture,[7c,d] was obtained in 76% yield by treating the reaction at 80 °C for 5 h. However, lower yield of **2d** (47%) was afforded from the reaction of **1a** with 4-methoxyaniline under identical reaction conditions, due to, probably, the reduced nucleophilicity of 4-methoxyaniline by the formation of complex between 4-methoxy moiety of 4-methoxyaniline and $BF_3{\cdot}Et_2O$. Hopefully, when a super-acid catalyst, triflic acid (TfOH), was selected to enhance the electrophilicity of dicarbonyl substrate **1a** through protonation with carbonyl oxygen,[13] both **2a** and **2d** were obtained in high yields. Thus, catalyzed by TfOH, a series of *N*-aryl-imino ketene *N,S*-acetals **2a**−**2w** were prepared from the pseudo three-component reaction of selected aryl amines with ketene *S,S*-acetals **1a** and **1b**, respectively (Table 1).

The above reaction (Table 1) showed that aniline and aryl amines bearing either an electron-donating or withdrawing substitute on *ortho*-, *meta*- or *para*-position of the phenyl ring are efficient nucleophiles to give the desired *N*-aryl-imino ketene *N,S*-acetals **2** generally in good to high yields. Hopefully, **2l** and **2t** can also be prepared in fair yields using 4-(trifluoromethyl)aniline, bearing a strong electron-withdrawing trifluoromethyl group, as the aryl amine component. Clearly, the pseudo three-component reaction provides a new and efficient access to α-imino ketene *N,S*-acetals in a single operation under mild reaction conditions starting from readily available starting materials.[7] In addition, the gram-scale synthesis of **2a** under identical conditions was proven successful (7.86 g, 30 mmol of **1a** to give 7.40 g of **2a**, 67% yield).

Table 1. Preparation of *N*-aryl-imino ketene *N,S*-acetals.



[a] 60% of TfOH was used.

α-Oxo ketene *N,S*-acetals, which easily isomerizes between (*Z*)- and (*E*)-configurations in both polar and non-polar media under various conditions via an imine intermediate,[7c,d] are versatile building blocks in organic synthesis.[7c-e] This isomerization is important for cyclization reactions due to the "equal contribution", for example the (*Z*)- and (*E*)-isomers of ketene *N,S*-acetals **2** with dense reactive sites.[7c]

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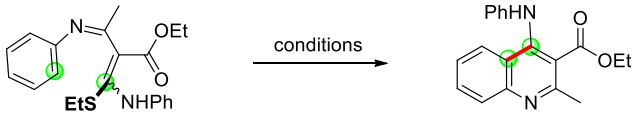
Table 2. Optimization of Reaction Conditions for Synthesis of 4-Anilinoquinolines. [a]

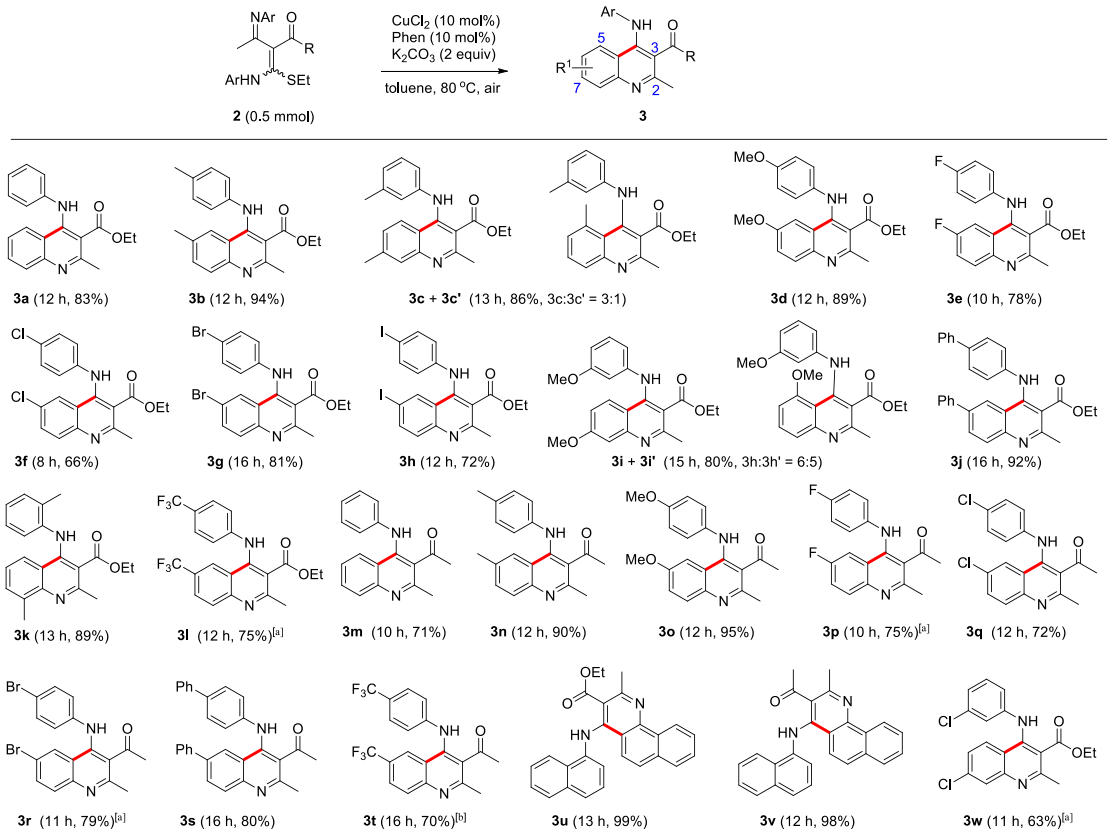


2a **3a**

Entry	Catalyst [mol%]	Ligand [mol%]	Base [equiv]	Solvent	Temp [°C]	*t* [h]	**3a** [%]
1	$Cu(OAc)_2$ (30%)	-	-	DMF	130	5.5	30
2	$Cu(OAc)_2$ (30%)	-	K_2CO_3 (2.0)	DMF	130	2.3	49
3	-	-	K_2CO_3 (2.0)	DMF	130	10	9
4	**$CuCl_2$ (10%)**	**Phen (10%)**	**K_2CO_3 (2.0)**	**toluene**	**80**	**12**	**83**
5	$CuCl_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	toluene	60	12	67
6	$CuBr_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	toluene	80	21	82
7	Cu_2O (10%)	Phen (10%)	K_2CO_3 (2.0)	toluene	80	28	86
8	CuI (10%)	Phen (10%)	K_2CO_3 (2.0)	toluene	80	14	83
9	CuCl (10%)	Phen (10%)	K_2CO_3 (2.0)	toluene	60	7	82
10	AgOAc (10%)	Phen (10%)	K_2CO_3 (2.0)	toluene	80	30	trace
11	$ZnCl_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	toluene	80	30	trace
12	$CuCl_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	DCE	80	16	78
13	$CuCl_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	THF	80	30	65
14	$CuCl_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	dioxane	80	23	57
15	$CuCl_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	$CHCl_3$	80	30	54
16	$CuCl_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	EtOH	80	30	20
17[b]	$CuCl_2$ (10%)	Phen (10%)	K_2CO_3 (2.0)	toluene	80	12	17

[a] General reaction conditions: **2a** (0.5 mmol), solvent 1 mL under aerobic conditions, and isolated yields of **3a**.
[b] The reaction was conducted under nitrogen atmosphere.

Table 3. Preparation of 4-Aminoquinolines **3a**–**3w**



[a] Reacted at 100 °C.
[b] Reacted at 110 °C.

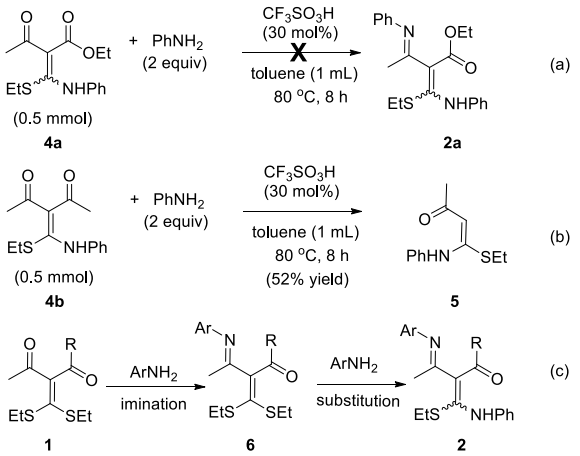
With ready access to *N*,*S*-acetals **2** established, the desulfitative cyclization of **2a** (without separation of the *E*- and *Z*-isomers) as a model to form the 4-aminoquinoline compound, ethyl 2-methyl-4-(phenylamino)quinoline-3-carboxylate **3a** (Table 2), was then examined. Under similar reaction conditions as our previous aerobic, Cu-catalyzed desulfitative C–C bond-forming reaction,[4a] catalyzed by $Cu(OAc)_2$ (mol 30%) in DMF at 130 °C in the open air for 5.5 h, **3a** was obtained in 30% yield (Table 2, entry 1). Pleasingly, the yield of **3a** reached up to 50% by adding K_2CO_3 (2 equiv) to the above reaction system (Table 2, entry 2). Whereas, in the absence of $Cu(OAc)_2$, the yield of **3a** decreased to less than 10% (Table 2, entry 3), indicating the role of both Cu(II) catalyst and a base for the formation of **3**.

Further optimization of reaction conditions showed that, catalyzed by anhydrous $CuCl_2$ (10 mol%), the reaction of **2a** proceeded efficiently in toluene in the presence of 1,10-phenanthroline (Phen, 10 mol%) and K_2CO_3 (2 equiv) in open air at 80 °C for 12 h (Table 2, entry 4). In this case, **3a** was obtained in 83% yield. Whereas, lower yield of **3a** was formed by reducing the reaction temperature to 60 °C (Table 2, entry 5). Under similar reaction conditions as in Table 2, entry 4, $CuBr_2$, Cu_2O (Table 2, entry 7), CuI (Table 2, entry 8), and CuCl (Table 2, entry 9) were efficient catalysts, respectively (Table 2, entries 6−9). As a comparison, AgOAc and $ZnCl_2$ were inefficient catalysts (Table 2, entries 10 and 11); the solvents, such as 1,2-dichloroethane (DCE), THF, dioxane, and chloroform (Table 2, entries 12−15) gave lower yields of **3a**.

It was found that, running the reaction of **2a** under the identical conditions as in Table 2, entry 4 but in a nitrogen atmosphere, **3a** was given in low yield (Table 2, entry 17). This result indicates that the existence of molecular oxygen plays a crucial role for desulfitative cyclization of **2** to give **3**. Thus, under the optimal conditions (Table 2, entry 4), a series of 4-anilinoquinolines **3** were prepared (Table 3).

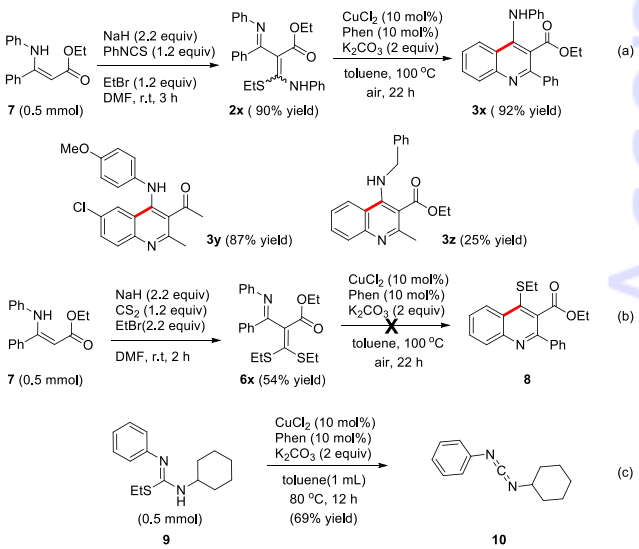
The experimental results (Table 3) showed that, all the *N*-aryl-imino ketene *N*,*S*-acetals **2a**−**2w** (Table 1) as substrates, including **2l** and **2t** bearing a strong electron-withdrawing trifluoromethyl group,[14] can give the desired 4-anilinoquinolines **3a**−**3w**[15] in high to excellent yields, though the nucleophilicity of the 4-(trifluoromethyl)aniline is reduced. In addition, the desulfitative cyclization of **2** proceeds chemoselectively, leaving ester (**3a**–**l**), acetyl (**3m**–**t**), and, aryl halides, especially, the aryl bromide (**3g** and **3r**) and aryl iodide (**3h**) functionalities intact. These reactive functional groups can be utilized for further modifications through Suzuki coupling and other reactions. Furthermore, the gram-scale synthesis of **3a** under identical conditions was proven successful (7.40 g, 20.10 mmol of **2a** to give 5.02 g of **3a**, 81% yield).

α-Imino ketene *N*,*S*-acetals have rarely been studied.[7c] It was found that, catalyzed either by $BF_3{\cdot}Et_2O$[12] or TfOH (Table 1), the reaction of α-oxo ketene *N*,*S*-acetal **4a**[7c] with aniline afforded a complex mixture instead of the desired **2a** (Scheme 2a). In the case of the reaction of **4b**[7c] with aniline, the sequential deacylation/amination product **5** was produced (Scheme 2b). These results tell that *N*-aryl-imino ketene *N*,*S*-acetals **2a**−**2w** should be formed via *N*-imino ketene *S*,*S*-acetals **6** as intermediate (Scheme 2c).



Scheme 2. Proposed mechanism for formation of imino ketene *N*,*S*-acetals **2a**−**2w**.

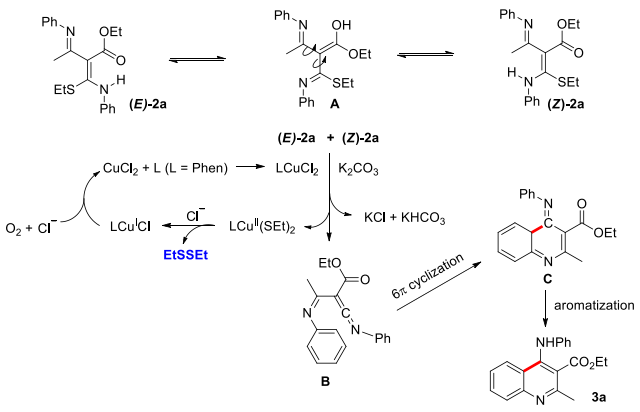
Catalyzed either by $BF_3{\cdot}Et_2O$ or TfOH (Table 1), the attempted isolation of **6a** from the reaction of **1a** with aniline was failed. Alternatively, 4-anilinoquinoline **3x**, bearing an aryl group at C2, was prepared in excellent yield with *N*-aryl-imino ketene *N*,*S*-acetal **2x** as substrate (Scheme 3a). In this case, **2x** was synthesized by the reaction of β-enamino ester **7**[16] with isothiocyanatobenzene. Similarly, **2y** and **2z** were prepared and 4-anilinoquinoline **3y** and **3z**, bearing a (*p*-methoxyphenyl)amino and benzyl amino group at C4, respectively, were also obtained.



Scheme 3. Preparation of ketene *N*,*S*-acetals **2x**−**2z**, 4-aminoquinolines **3x**−**3z**, and carbodiimide **10**.

The successful synthesis of 4-aminoquinolines **3x**−**3z** starting from β-enamino ester **7** provides an alternative route to 4-aminoquinolines and an experimental evidence to support the formation of **2a**−**2w** via *N*-imino ketene *S*,*S*-acetal intermediate **6** (Scheme 2c). Furthermore, *N*-imino ketene *S*,*S*-acetal **6x** was prepared and subjected to the reaction conditions for the synthesis of 4-aminoquinolines **3** (Scheme 3b). In this case, however, 4-ethylthio quinoline **8** could not be obtained and **6x** was recovered in 83% yield. These results show that the *N*,*S*-acetal moiety is crucial for the desulfitative cyclization reaction. Indeed, carbodiimide **10** was obtained from the Cu(II)-catalyzed elimination of EtSH of carbamimidothioate **9** (Scheme 3c).

In addition, running the reaction of **9** under the identical conditions as in Table 2, entry 4 but in a nitrogen atmosphere gave low yields of **10** (10%), indicating that the existence of molecular oxygen in air plays a crucial role for elimination of EtSH from **9** to afford **10**. Based on above results (Table 2, 3 and Scheme 3) and related reports,[4a,17,18] a mechanism for the formation of 4-anilinoquinolines **3** was proposed (Scheme 4, with **3a** as an example).



Scheme 4. Proposed mechanism for formation of 4-aminoquinolines **3**.

According to the nature of the reversible isomerization of ketene *N*,*S*-acetals,[7c,d] and elimination of EtSH from **9** (Scheme 3c), a base-promoted elimination of EtSH from imino ketene *N*,*S*-acetal **2a** would occur along with the generation of ketenimine intermediate **B** and $LCu(SEt)_2$ (L = Phen). Ketenimine (**B**) undergoes 6π electrocyclization[17] followed by aromatization to give the thermodynamically favored 4-anilinoquinolines **3**. At the same time, serving as a crucial step forward, the eliminated EtSH is to be oxidized by Cu(II) to form the disulfide,[18] $(EtS)_2$, as the by-product along with formation of a Cu(I) species. In the presence of molecular oxygen as the oxidant, catalytic system $LCu^{II}Cl_2$ is to be regenerated for the next cycle through oxidation of Cu(I) species (Scheme 4). This mechanism can also be used to explain the efficiency of Cu(I) salts as the catalysts (Table 2, entries 8 and 9).

Conclusion

In conclusion, an extremely simple and efficient pathway to construct substituted 4-anilinoquinolines via Cu(II)-catalyzed desulfitative 6π electrocyclization with disulfide as the by product was developed. In this unprecedented reaction, various imino ketene *N*,*S*-acetals, as starting materials, can be prepared, generally, in good to high yields by either the acid-catalyzed three-component reaction of arylamines with acetyl ketene *S*,*S*-acetals or by the reaction of β-enamino esters with isothiocyanates under mild reaction conditions. The Cu(II)-catalyzed desulfitative cyclization of *N*-aryl-imino ketene *N*,*S*-acetals can tolerate a wide range of reactive functional groups and incorporate various functional groups at C2−C8 positions of 4-anilinoquinolines as products. Further works focused on expansion of this new strategy are in progress.

Experimental Section

General procedure for the synthesis of 2 (taking **2a** as an example). To the solution of ethyl 2-[bis(ethylthio)methylene]-3-oxobutanoate (131 mg, 0.50 mmol) and aniline (140 mg, 1.50 mmol) in toluene (1.0 mL) was added trifluoromethanesulfonic acid (13.3 μL, 0.15 mmol), and stirred at 80 °C. After the reaction was finished as indicated by TLC (reaction time, 3.2 h),the resulting mixture was allowed to cool to room temperature and slowly poured into saturated aqueous NaCl (20 mL), and extracted with dichloromethane (20 mL × 3). The combined organic phase was dried over anhydrous $Na_2SO_4$and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel (PE/EtOAc = 60:1) to afford **2a** (134 mg, 73% yield) as yellowish solid.

(3*E*)-Ethyl 2-(ethylthio(phenylamino)methylene)-3-(phenylimino)butanoate(2a) [*E*/*Z*=1/4]: yield: 134 mg (73%); yellowish solid; mp 45–46 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2a***): δ = 10.85 (s, 1H), 7.27–7.21 (m, 4H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 2H), 6.81 (d, *J* = 7.5 Hz, 2H), 4.23–4.15 (m, 2H), 3.13–3.00 (m, 2H), 1.93 (s, 3H), 1.38 (t, *J* = 7.5 Hz, 3H), 1.31 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2a***): δ = 11.12 (s, 1H), 7.37–7.34 (m, 4H), 7.26–7.20 (m, 1H), 7.15–7.09 (m, 3H), 6.93 (d, *J* = 7.5 Hz, 2H), 4.26 (q, *J* = 7.5 Hz, 2H), 2.75 (q, *J* = 7.5 Hz, 2H), 2.18 (s, 3H), 1.34 (t, *J* = 7.5 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.7, 165.5, 157.8, 150.9, 138.4, 129.2, 129.0, 128.9, 128.4, 125.9, 125.6, 125.4, 125.2, 123.9, 123.2, 120.1, 119.3, 96.0, 59.7, 59.6, 27.0, 25.3, 17.9, 17.2, 14.4(2), 13.9. HR-MS (ESI): *m/z* = 369.1635, calcd. for $C_{21}H_{25}N_2O_2S$ $(M+H)^+$: 369.1631.

(3*E*)-Ethyl 2-(ethylthio(*p*-tolylamino)methylene)-3-(*p*-tolylimino)butanoate(2b) [*E*/*Z*=1:3]: yield: 164 mg (83%); yellowish solid; mp 63–64 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2b***): δ = 10.77 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 6.69 (d, *J* = 8.0 Hz, 2H), 4.22–4.15 (m, 2H), 3.12–2.98 (m, 2H), 2.30 (s, 3H), 2.29 (s, 3H), 1.90 (s, 3H), 1.37 (t, *J* = 7.5 Hz, 3H), 1.31 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2b***): δ = 11.02 (s, 1H), 7.18–7.15 (m, 4H), 7.02–7.00 (m, 2H), 6.84–6.81 (m, 2H), 4.25 (q, *J* = 7.0 Hz, 2H), 2.74 (q, *J* = 7.5 Hz, 2H), 2.35 (s, 3H), 2.34 (s, 3H), 2.14 (s, 3H), 1.34 (d, *J* = 7.0 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.2, 167.8, 166.9, 165.1, 158.9, 158.1, 148.2, 148.0, 135.8, 135.7, 135.5, 133.4, 132.4, 129.7, 129.5, 129.0, 125.5, 125.2, 119.9, 119.2, 96.7, 95.5, 59.6, 59.5, 59.4, 26.9, 25.2, 21.0, 20.9, 20.8(2), 17.8, 17.1,

14.5, 14.4(2), 13.9. HR-MS (ESI): *m/z* = 397.1951, calcd. for $C_{23}H_{29}N_2O_2S$ $(M+H)^+$: 397.1944.

(3*E*)-Ethyl 2-(ethylthio(*m*-tolylamino)methylene)-3-(*m*-tolylimino)butanoate(2c) [*E*/*Z*=1:4]: yield: 152 mg (77%); yellow viscous liquid; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-**2c**): δ = 10.82 (s, 1H), 7.15–7.10 (m, 2H), 6.95 (d, *J* = 7.0 Hz, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 6.72–6.70 (m, 2H), 6.64 (s, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 4.40–4.05 (m, 2H), 2.99–3.12 (m, 2H), 2.28 (s, 3H), 2.27 (s, 3H), 1.96 (s, 3H), 1.37 (t, *J* = 7.5 Hz, 3H), 1.32 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-**2c**): δ = 11.09 (s, 1H), 7.25–7.21 (m, 2H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.95–6.91 (m, 3H), 6.72–6.70 (m, 2H), 4.28–4.12 (m, 2H), 2.74 (q, *J* = 7.5 Hz, 2H), 2.35 (s, 3H), 2.34 (s, 3H), 2.19 (s, 3H), 1.35 (t, *J* = 7.5 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.0, 167.6, 166.6, 165.1, 158.5, 157.8, 150.9, 150.5, 139.0, 138.8, 138.6, 138.3, 137.8, 128.8, 128.7, 128.1, 126.5, 126.3, 125.9, 125.7, 124.6, 123.8, 122.3, 122.0, 120.7, 119.8, 116.7, 116.2, 97.0, 95.9, 59.5, 59.4, 26.9, 25.2, 21.4, 21.3, 21.2, 21.1, 17.8, 17.1, 14.4(2), 14.3, 13.8. HR-MS (ESI): *m/z* = 335.1766, calcd. for $C_{21}H_{23}N_2O_2$ $(M\text{-}SEt)^+$: 335.1754.

(3*E*)-Ethyl 2-(ethylthio(4-methoxyphenylamino)methylene)-3-(4-methoxyphenylimino)butanoate(2d) [*E*/*Z*=2:7]: yield: 165 mg (77%); yellow viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-**2d**): δ = 10.68 (s, 1H), 6.94–6.72 (m, 8H), 4.30–4.13 (m, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 2.97–3.13 (m, 2H), 1.82 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.30 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-**2d**): δ = 10.92 (s, 1H), 7.06 (d, *J* = 8.8 Hz, 2H), 6.94–6.72 (m, 6H), 3.80 (s, 3H), 3.79 (s, 3H), 2.75 (q, *J* = 7.5 Hz, 2H), 2.09 (s, 3H), 1.36–1.34 (m, 3H), 1.19 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.2, 167.9, 165.2, 159.4, 158.6, 157.9, 157.7, 156.3, 155.7, 152.7, 144.0, 143.8, 139.9, 131.2, 127.3, 127.0, 121.3, 120.6, 116.3, 114.7, 114.3, 114.2, 114.1, 113.7, 95.1, 59.5, 59.4, 55.6, 55.4, 55.3, 26.9, 25.2, 17.6, 17.0, 14.4, 13.9. HR-MS (ESI): *m/z* = 429.1832, calcd. for $C_{23}H_{29}N_2O_4S$ $(M+H)^+$: 429.1843.

(3*E*)-Ethyl 2-(ethylthio(4-fluorophenylamino)methylene)-3-(4-fluorophenylimino)butanoate(2e) [*E*/*Z*=1:5]: yield: 167 mg (86%); yellowish solid; mp 83–84 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-**2e**): δ = 10.76 (s, 1H), 6.99–6.92 (m, 4H), 6.90–6.88 (m, 2H), 6.78–6.75 (m, 2H), 4.20 (q, *J* = 7.5 Hz, 2H), 3.13–2.99 (m, 2H), 1.85 (s, 3H), 1.37 (t, *J* = 7.5 Hz, 3H), 1.30 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-**2e**): δ = 11.01 (s, 1H), 7.12–7.09 (m, 2H), 7.07–7.03 (m, 4H), 6.90–6.88 (m, 2H), 4.26 (q, *J* = 7.5 Hz, 2H), 2.76 (q, *J* = 7.5 Hz, 2H), 2.11 (s, 3H), 1.34 (t, *J* = 7.5 Hz, 3H), 1.19 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 167.5, 166.1, 160.5 (d, *J* =244.6 Hz), 160.7 (d, *J* =244.9 Hz), 160.5, 160.1, 158.6, 158.1, 157.9, 146.7 (d, *J* = 2.8 Hz), 146.4 (d, *J* = 2.8 Hz), 134.3 (d, *J* = 2.8 Hz), 134.2 (d, *J* = 2.8 Hz), 127.4 (d, *J* = 8.4 Hz), 127.2 (d, *J* = 8.4 Hz), 121.2 (d, *J* = 7.9 Hz), 120.6 (d, *J* = 7.9 Hz), 115.8 (d, *J* = 22.1 Hz), 115.0 (d, *J* = 22.1 Hz), 95.6(2), 59.5, 26.9, 25.2, 17.5, 16.8, 14.3(2), 14.2, 13.7. HR-MS (ESI): *m/z* = 405.1428, calcd. for $C_{21}H_{23}F_2N_2O_2S$ $(M+H)^+$: 405.1443.

(3*E*)-Ethyl 2-((4-chlorophenylamino)(ethylthio)methylene)-3-(4-chlorophenylimino)butanoate(2f) [*E*/*Z*=1:3]: yield: 164 mg (75%); white solid; mp 96–97 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-**2f**): δ = 10.84 (s, 1H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 2H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.16–2.94 (m, 2H), 1.91 (s, 3H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-**2f**): δ = 11.08 (s, 1H), 7.32 (d, *J* = 8.5 Hz, 4H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.25 (q, *J* = 7.5 Hz, 2H), 2.75 (q, *J* = 7.5 Hz, 2H), 2.14 (s, 3H), 1.33 (t, *J* = 7.5 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.9, 167.7, 167.4, 166.2, 157.9, 157.3, 149.3, 148.8, 136.8, 136.7, 131.4, 131.2, 129.2, 129.1, 129.0, 128.4, 128.3, 126.5, 126.3, 121.3, 120.7, 97.7, 96.2, 59.8, 59.7, 27.0, 25.3, 17.7, 17.0, 14.3, 14.2, 13.7. HR-MS (ESI): *m/z* = 437.0841, calcd. for $C_{21}H_{23}Cl_2N_2O_2S$ $(M+H)^+$: 437.0852.

(3*E*)-Ethyl 2-((4-bromophenylamino)(ethylthio)methylene)-3-(4-bromophenylimino)butanoate(2g) [*E*/*Z*=1:5]: yield: 194 mg (74%); yellowish solid; mp 78–80 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-**2g**): δ = 10.83 (s, 1H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 2H), 6.67 (d, *J* = 8.5 Hz, 2H), 4.18 (q, *J* = 7.0 Hz, 2H), 3.12–3.00 (m, 2H), 1.91 (s, 3H), 1.36 (t, *J* = 7.5 Hz, 3H), 1.30 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-**2g**): δ = 11.07 (s, 1H), 7.48–7.45 (m, 4H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.82–6.79 (m, 2H), 4.25 (q, *J* = 7.0 Hz, 2H), 2.74 (q, *J* = 7.5 Hz, 2H), 2.14 (s, 3H), 1.33 (t, *J* = 7.0 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.5, 166.3, 157.9, 157.3, 149.8, 149.3, 137.3, 132.3, 132.2, 132.1, 131.5, 126.8, 126.7, 121.8, 121.2, 119.1, 117.0, 116.2, 96.4, 59.9, 59.8, 27.1, 25.4, 17.8, 17.1, 14.4, 14.3, 13.8. HR-MS (ESI): *m/z* = 524.9831, calcd. for $C_{21}H_{23}Br_2N_2O_2S$ $(M+H)^+$: 524.9842.

(3*E*)-Ethyl 2-(ethylthio(4-iodophenylamino)methylene)-3-(4-iodophenylimino)butanoate(2h) [*E*/*Z*=1:5]: yield: 205 mg (66%); yellowish solid; mp 90–91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-**2h**): δ = 10.84 (s, 1H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 2H), 6.69 (d, *J* = 8.5 Hz, 2H), 6.55 (d, *J* = 8.5 Hz, 2H), 4.21–4.14 (m, 2H), 3.10–2.98 (m, 2H), 1.92 (s, 3H), 1.36 (t, *J* = 7.5 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-**2h**): δ = 11.08 (s, 1H), 7.67–7.64 (m, 4H), 6.87 (d, *J* = 8.5 Hz, 2H), 6.69 (d, *J* = 8.5 Hz, 2H), 4.31–4.22 (m, 2H), 2.77–2.69 (m, 2H), 2.15 (s, 3H), 1.35–1.31 (m, 3H), 1.18 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 167.4, 166.1, 157.7, 157.0, 150.4, 138.2, 138.0, 137.9, 137.4, 137.3, 126.9, 126.7, 122.2, 121.5, 119.9, 96.4, 89.8, 86.9, 59.8, 27.1, 25.4, 17.8, 17.1, 14.4, 14.3, 13.8. HR-MS (ESI): *m/z* = 642.9385, calcd. for $C_{21}H_{22}I_2N_2NaO_2S$ $(M+Na)^+$: 642.9384.

(3*E*)-Ethyl 2-(ethylthio(3-methoxyphenylamino)methylene)-3-(3-methoxyphenylimino)butanoate(2i) [*E*/*Z*=1:4]: yield: 161 mg (75%); yellowish viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-**2i**): δ = 10.84 (s, 1H), 7.18–7.11 (m, 2H), 6.73–6.63 (m, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 1H), 6.47 (s, 1H), 6.40–6.37 (m, 2H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 3H), 3.73 (s, 3H), 3.13–3.00 (m, 2H), 1.98 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.32 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-**2i**): δ = 11.09 (s, 1H), 7.30–7.24 (m, 2H), 6.77–6.67 (m, 4H), 6.57–6.52 (m, 1H), 6.48 (s, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 3.78 (s, 3H), 2.74 (q, *J* = 7.2 Hz, 2H), 2.20 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.9, 167.5, 166.9, 165.5, 160.1, 159.9, 159.7, 158.3, 157.6, 152.1, 151.6, 139.4, 129.7, 129.6, 129.5, 129.0, 117.5, 117.2, 112.4, 111.6, 111.3, 111.1, 110.9, 110.6, 109.0, 108.8, 105.6, 105.2, 97.2, 96.1, 59.6, 59.5, 55.2, 55.1, 55.0, 54.9, 26.9, 25.2, 17.8, 17.1, 14.3(2), 14.0, 13.8. HR-MS (ESI): *m/z* = 429.1837, calcd. for $C_{23}H_{29}N_2O_4S$ $(M+H)^+$: 429.1843.

(3*E*)-Ethyl 2-((biphenyl-4-ylamino)(ethylthio)methylene)-3-(biphenyl-4-ylimino)butanoate(2j) [*E*/*Z*=2:9]: yield: 182 mg (70%); yellowish solid; mp 46–48 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-**2j**): δ = 10.97 (s, 1H), 7.62–7.57 (m, 3H), 7.51 (d, *J* = 8.0 Hz, 4H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.41–7.37 (m, 4H), 7.31–7.26 (m, 1H), 6.96 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 4.31–4.20 (m, 2H), 3.27–2.95 (m, 2H), 2.02 (s, 3H), 1.40 (t, *J* = 7.5 Hz, 3H), 1.34 (t, *J* = 7.0 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-**2j**): δ = 11.21 (s, 1H), 7.65–7.54 (m, 4H), 7.43–7.37 (m, 4H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.31–7.26 (m, 5H), 7.20–7.18 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 4.37–4.14 (m, 2H), 2.78 (q, *J* = 7.5 Hz, 2H), 2.26 (s, 3H), 1.37 (d, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 167.7, 167.0, 165.6, 158.3, 157.6, 150.1, 149.6, 140.8, 139.9, 138.6, 138.3, 137.5(2), 136.8, 135.9, 128.8, 128.7, 128.6, 127.7(2), 127.5, 127.3, 127.1, 126.8, 126.7(2), 126.6, 125.4, 125.1, 120.5, 119.8, 97.5, 96.2, 59.7, 59.6, 27.1, 25.4, 17.9, 17.3, 14.5, 14.4(2), 13.9.

HR-MS (ESI): *m/z* = 521.2245, calcd. for $C_{33}H_{33}N_2O_2S$ $(M+H)^+$: 521.2257.

(3*E*)-Ethyl 2-(ethylthio(*o*-tolylamino)methylene)-3-(*o*-tolylimino)butanoate(2k) [*E*/*Z*=1:1]: yield: 91 mg (46%); yellowish viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-***2k***): δ = 10.64 (s, 1H), 7.25–7.07 (m, 4H), 7.04–7.00 (m, 2H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 7.6 Hz, 1H), 4.21–4.13 (m, 2H), 3.16–3.05 (m, 2H), 2.25 (s, 6H), 1.99 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-***2k***): δ = 10.95 (s, 1H), 7.25–7.07 (m, 6H), 6.94–6.88 (m, 2H), 4.26 (q, *J* = 6.8 Hz, 2H), 2.74 (q, *J* = 7.2 Hz, 2H), 2.31 (s, 3H), 2.10 (s, 3H), 1.73 (s, 3H), 1.34 (t, *J* = 6.8 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 167.8, 166.9, 163.7, 159.0(2), 149.1, 148.2, 137.0, 136.9, 134.5, 134.0, 130.7, 130.5, 130.3, 129.9, 129.8, 127.4, 127.1, 126.7, 126.6, 126.5, 126.4, 126.2, 126.1, 125.5, 123.8, 123.3, 118.7, 118.2, 96.1, 94.7, 59.4, 59.3, 26.7, 24.9, 17.9(2), 17.4(2), 17.3, 16.8, 14.4, 14.3, 14.2(2). HR-MS (ESI): *m/z* = 397.1937, calcd. for $C_{23}H_{29}N_2O_2S$ $(M+H)^+$: 397.1944.

(3*E*)-Ethyl 2-(ethylthio(4-(trifluoromethyl) phenylamino)methylene)-3-(4-(trifluoromethyl) phenylimino)butanoate(2l) [*E*/*Z*=1:6]: yield: 86 mg (34%); yellowish viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-***2l***): δ =11.06 (s, 1H), 7.57–7.50 (m, 4H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.17–3.00 (m, 2H), 2.03 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H), 1.34 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-***2l***): δ =11.30 (s, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.57–7.55 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 4.30–4.24 (m, 2H), 2.76–2.74 (m, 2H), 2.26 (s, 3H), 1.39–1.33 (m, 3H), 1.23–1.20 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ =167.4, 166.6, 156.6, 154.0, 141.5, 127.2 (q, *J* = 32.6 Hz), 126.3 (q, *J* = 3.9 Hz), 125.8 (q, *J* = 4.1 Hz), 124.2, 123.3, 122.8, 120.5, 120.1, 119.5, 97.6, 60.1, 26.4, 25.5, 18.0, 14.4, 13.7. ^{19}F NMR (470 MHz, $CDCl_3$): δ = -63.8(2), -64.2, -64.3. HR-MS (ESI): *m/z* = 527.1196, calcd. for $C_{23}H_{22}F_6N_2NaO_2S$ $(M+Na)^+$: 527.1198.

(4*E*)-3-(Ethylthio(phenylamino)methylene)-4-(phenylimino)pentan-2-one(2m) [*E*/*Z*=1:3]: yield: 106 mg (63%); yellowish solid; mp 76–77 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2m***): δ = 13.25 (s, 1H), 7.33–7.25 (m, 4H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.97(d, *J* = 7.5 Hz, 2H), 6.80 (m, *J* = 7.5 Hz, 2H), 3.21–2.99 (m, 2H), 2.24 (s, 3H), 1.98 (s, 3H), 1.40 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2m***): δ = 13.38 (s, 1H), 7.41–7.38 (m, 4H), 7.27–7.25 (m, 1H), 7.16–7.13 (m, 3H), 6.94 (d, *J* = 7.0 Hz, 2H), 2.76–2.72 (m, 2H), 2.38 (s, 3H), 2.19 (s, 3H), 1.20 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.3, 167.5, 160.0, 149.9, 137.8, 129.2, 129.1(2), 128.7, 126.5, 126.3, 125.6, 125.4, 124.3, 123.6, 120.4, 119.1, 108.5, 107.2, 28.1, 27.8, 27.6, 25.5, 18.1, 17.1, 14.3, 13.8. HR-MS (ESI): *m/z* = 361.1345, calcd. for $C_{20}H_{22}N_2NaOS$ $(M+Na)^+$: 361.1345.

(4*E*)-3-(Ethylthio(*p*-tolylamino)methylene)-4-(*p*-tolylimino)pentan-2-one(2n) [*E*/*Z*=2:5]: yield: 121 mg (66%); yellowish solid; mp 85–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-***2n***): δ = 13.19 (s, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.06–7.38 (m, 2H), 6.88–6.86 (m, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 3.13–3.03 (m, 2H), 2.32 (s, 3H), 2.29 (s, 3H), 2.20 (s, 3H), 1.96 (s, 3H), 1.39 (t, *J* = 7.6 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-***2n***): δ = 13.31 (s, 1H), 7.20–7.17 (m, 4H), 7.07–7.02 (m, 2H), 6.87–6.83 (m, 2H), 2.75–2.71 (m, 2H), 2.37–2.33 (m, 9H), 2.15 (s, 3H), 1.19 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.3, 193.1, 168.9, 166.9, 160.3, 147.6, 147.3, 136.3, 136.1, 135.2, 135.1, 133.7, 133.0, 129.8, 129.6(2), 129.2, 125.4, 125.3, 120.4, 119.0, 108.3, 107.0, 28.0, 27.7, 27.5, 25.3, 20.9(3), 20.8, 17.9, 17.0, 14.3, 13.8. HR-MS (ESI): *m/z* = 389.1644, calcd. for $C_{22}H_{26}N_2NaOS$ $(M+Na)^+$: 389.1658.

(4*E*)-3-(Ethylthio(4-methoxyphenylamino)methylene)-4-(4-methoxyphenylimino)pentan-2-one(2o) [*E*/*Z*=1:3]: yield: 151 mg (76%); yellowish solid; mp 120–121 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2o***): δ = 13.18 (s, 1H), 6.91–6.79 (m, 8H), 3.71 (s, 3H), 3.70 (s, 3H), 3.12–3.02 (m, 2H), 2.20 (s, 3H), 1.92 (s, 3H), 1.37 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2o***): δ = 13.28 (s, 1H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.91–6.79 (m, 6H), 3.74 (s, 3H), 3.73 (s, 3H), 2.76–2.60 (m, 2H), 2.35 (s, 3H), 2.12 (s, 3H), 1.17 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.6, 192.4, 168.4, 165.9, 160.2, 160.1, 157.6, 157.5, 156.0, 155.6, 142.9, 142.4, 130.0, 126.5, 126.3, 121.5, 120.0, 113.9, 113.8, 113.4, 107.8, 106.3, 54.8(2), 54.7(2), 27.5, 27.2, 27.0, 24.8, 17.2, 16.5, 13.9, 13.5. HR-MS (ESI): *m/z* = 399.1737, calcd. for $C_{22}H_{27}N_2O_3S$ $(M+H)^+$: 399.1737.

(4*E*)-3-(Ethylthio(4-fluorophenylamino)methylene)-4-(4-fluorophenylimino)pentan-2-one(2p) [*E*/*Z*=1:3]: yield: 125 mg (67%); white solid; mp 88–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-***2p***): δ = 13.15 (s, 1H), 7.10–6.94 (m, 6H), 6.79–6.74 (m, 2H), 3.14–3.03 (m, 2H), 2.22 (s, 3H), 1.90 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-***2p***): δ = 13.26 (s, 1H), 7.17–6.93 (m, 6H), 6.91–6.88 (m, 2H), 2.76–2.72 (m, 2H), 2.35 (s, 3H), 2.12 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.6, 193.5, 169.9, 168.0, 161.0 (d, *J* =246.3 Hz), 160.2, 160.1, 159.4 (d, *J* =241.3 Hz), 145.8 (d, *J* =2.5 Hz), 133.7 (d, *J* =2.5 Hz), 127.5 (d, *J* =8.8 Hz), 127.3 (d, *J* =8.8 Hz), 121.9 (d, *J* =7.5 Hz), 120.6 (d, *J* =7.5 Hz), 116.3, 116.1(2), 116.0, 115.9, 115.8, 115.5, 115.3, 108.6, 106.9, 28.0, 27.8, 27.6, 25.5, 17.8, 17.0, 14.3, 13.8. HR-MS (ESI): *m/z* = 397.1150, calcd. for $C_{20}H_{20}F_2N_2NaOS$ $(M+Na)^+$: 397.1157.

(4*E*)-3-((4-Chlorophenylamino)(ethylthio)methylene)-4-(4-chlorophenylimino)pentan-2-one(2q) [*E*/*Z*=1:3]: yield: 134 mg (66%); white solid; mp 121–122 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2q***): δ = 13.23 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 8.0 Hz, 2H), 3.15–3.02 (m, 2H), 2.21 (s, 3H), 1.95 (s, 3H), 1.39 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2q***): δ = 13.33 (s, 1H), 7.36–7.33 (m, 4H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 2.75–2.72 (m, 2H), 2.35 (s, 3H), 2.15 (s, 3H), 1.20 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.7, 193.5, 169.8, 168.3, 159.5, 148.5, 148.3, 136.3, 136.2, 132.1, 131.9, 129.4, 129.2, 128.9, 128.8, 126.7, 126.6, 121.8, 120.5, 108.8, 107.2, 28.1, 27.8, 27.6, 25.5, 17.9, 17.0, 14.2, 13.7. HR-MS (ESI): *m/z* = 429.0566, calcd. for $C_{20}H_{20}Cl_2N_2NaOS$ $(M+Na)^+$: 429.0566.

(4*E*)-3-((4-Bromophenylamino)(ethylthio)methylene)-4-(4-bromophenylimino)pentan-2-one(2r) [*E*/*Z*=2:7]: yield: 168 mg (68%); yellowish solid; mp 106–108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-***2r***): δ = 13.24 (s, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.36 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.67 (d, *J* = 8.4 Hz, 2H), 3.13–2.99 (m, 2H), 2.21 (s, 3H), 1.97 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-***2r***): δ = 13.34 (s, 1H), 7.49–7.46 (m, 4H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 2.74–2.71 (m, 2H), 2.35 (s, 3H), 2.15 (s, 3H), 1.19 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.4, 193.1, 169.5, 168.1, 159.1, 159.0, 148.7, 148.6, 136.5, 136.5, 132.1, 132.0, 131.9, 131.5, 126.7, 126.6, 122.0, 120.7, 119.6, 119.4, 117.0, 116.5, 108.6, 107.0, 27.9, 27.6, 27.4, 25.3, 17.7, 16.8, 14.1, 13.5. HR-MS (ESI): *m/z* = 516.9549, calcd. for $C_{20}H_{20}Br_2N_2NaOS$ $(M+Na)^+$: 516.9555.

(4*E*)-3-((Biphenyl-4-ylamino)(ethylthio)methylene)-4-(biphenyl-4-ylimino)pentan-2-one(2s) [*E*/*Z*=2:7]: yield: 152 mg (62%); yellowish solid; mp 124–125 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2s***): δ = 13.40 (s, 1H), 7.63–7.40 (m, 8H), 7.41–7.35 (m, 4H), 7.28 (t, *J* = 7.5 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* =8.0 Hz, 2H), 3.17–3.05 (m, 2H), 2.30 (s, 3H), 2.05 (s, 3H), 1.43–1.39 (m, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2s***): δ = 13.50 (s, 1H), 7.63–7.45 (m, 11H), 7.41–7.35 (m, 1H), 7.33–7.25 (m, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.06–7.03 (m, 2H), 2.77–7.73 (m, 2H), 2.42 (s, 3H), 2.24 (s, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.3, 193.1, 168.9, 167.4, 159.6, 149.2, 148.9, 140.4, 140.3, 139.6, 138.9, 138.7, 136.9, 136.7,

136.2, 128.6(2), 128.5, 127.6, 127.4, 127.2(2), 126.7(2), 126.6, 126.5, 125.4, 125.2, 120.9, 119.4, 108.7, 107.3, 28.0, 27.5, 25.4, 17.9, 17.0, 14.2, 13.7(2). HR-MS (ESI): *m/z* = 491.2157, calcd. for $C_{32}H_{31}N_2OS$ $(M+H)^+$: 491.2152.

(4*E*)-3-(Ethylthio(4-(trifluoromethyl)phenylamino) methylene)-4-(4-(trifluoromethyl)phenylimino)pentan-2-one(2t) [*E*/*Z*=1:4]: yield: 97 mg (41%); white solid; mp 109–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-***2t***): δ = 13.39 (s, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 3.17–3.04 (m, 2H), 2.26 (s, 3H), 2.06 (s, 3H), 1.41 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-***2t***): δ = 13.51 (s, 1H), 7.70–7.65 (m, 4H), 7.27–7.25 (m, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 2.80–2.70 (m, 2H), 2.40 (s, 3H), 2.26 (s, 3H), 1.23 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.9, 169.0, 158.9, 153.0, 141.0, 128.0 (d, *J* = 32.6 Hz), 126.4 (q, *J* = 4.4 Hz), 126.0 (q, *J* = 3.9 Hz), 125.0, 120.4, 119.3, 108.0, 28.2, 28.0, 27.8, 25.7, 18.2, 17.2, 14.2, 13.6. ^{19}F NMR (470 MHz, $CDCl_3$): δ = -63.9, -64.3, -64.4. HR-MS (ESI): *m/z* = 497.1088, calcd. for $C_{22}H_{20}F_6N_2NaOS$ $(M+Na)^+$: 497.1093.

(3*E*)-Ethyl 2-(ethylthio(naphthalen-1-ylamino)methylene)-3-(naphthalen-1-ylimino)butanoate(2u) [*E*/*Z*=2:5]: yield: 138 mg (59%); yellowish solid; mp 76–77 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2u***): δ = 10.98 (s, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.67–7.21 (m, 9H), 7.04 (d, *J* = 7.0 Hz, 1H), 6.86 (d, *J* = 7.0 Hz, 1H), 4.25–3.97 (m, 2H), 3.32–3.20 (m, 2H), 1.68 (s, 3H), 1.49 (t, *J* = 7.0 Hz, 3H), 1.17 (t, *J* = 7.0 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2u***): δ = 11.40 (s, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.90–7.79 (m, 2H), 7.77–7.73 (m, 1H), 7.67–7.21 (m, 8H), 6.94 (d, *J* = 7.0 Hz, 1H), 4.41 (q, *J* = 7.0 Hz, 2H), 2.79 (q, *J* = 7.5 Hz, 2H), 2.19 (s, 3H), 1.49 (t, *J* = 7.0 Hz, 3H), 1.17 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.4, 167.9, 165.7, 160.2, 159.9, 146.9, 146.6, 134.2(2), 134.1, 134.0, 130.3, 128.2, 128.0, 127.9, 127.7, 127.6, 127.2, 126.9, 126.7, 126.5, 126.2, 126.0, 125.7, 125.6(2), 125.2, 125.1, 124.8, 124.2, 124.1, 124.0, 123.9, 123.7, 123.3, 122.4, 122.2, 113.9, 97.0, 95.3, 59.9, 59.5, 27.0, 25.4, 17.8, 17.1, 14.5, 14.4, 14.3, 14.2. HR-MS (ESI): *m/z* = 491.1771, calcd. for $C_{29}H_{28}N_2NaO_2S$ $(M+Na)^+$: 491.1764.

(4*E*)-3-(Ethylthio(naphthalen-1-ylamino)methylene)-4-(naphthalen-1-ylimino)pentan-2-one(2v) [*E*/*Z*=2:7]: yield: 134 mg (61%); white solid; mp 45–46 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2v***): δ = 13.43 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.49–7.39 (m, 5H), 7.36–7.33 (m, 2H), 7.11 (d, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 1H), 3.38–3.22 (m, 2H), 2.31 (s, 3H), 1.69 (s, 3H), 1.51 (t, *J* = 7.5 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2v***): δ = 13.77 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.94–7.89 (m, 2H), 7.87–7.82 (m, 2H), 7.67–7.63 (m, 1H), 7.60–7.53 (m, 2H), 7.50–7.38 (m, 5H), 7.04 (d, *J* = 7.0 Hz, 1H), 2.85–2.75 (m, 2H), 2.59 (s, 3H), 2.23 (s, 3H), 1.19 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.9, 167.8, 162.4, 145.3, 134.2, 134.0, 133.9, 129.9, 128.3, 128.1, 127.9, 127.6, 127.2, 126.9, 126.7, 126.5, 126.2, 126.0, 125.6, 125.4, 125.1, 124.5, 124.0, 123.9, 123.5, 122.8, 122.5, 122.3, 114.5, 113.9, 106.7, 28.4, 27.6, 25.6, 17.9, 17.5, 14.3. HR-MS (ESI): *m/z* = 461.1657, calcd. for $C_{28}H_{26}N_2NaOS$ $(M+Na)^+$: 461.1658.

(4*E*)-3-((3-Chlorophenylamino)(ethylthio)methylene)-4-(3-chlorophenylimino)pentan-2-one(2w) [*E*/Z=1:6]: yield: 131 mg (60%); yellow viscous liquid; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2w***): δ = 10.90 (s, 1H), 7.23–7.09 (m, 3H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.94 (s, 1H), 6.86–6.76 (m, 2H), 6.66 (d, *J* = 8.0 Hz, 1H), 4.35–4.08 (m, 2H), 3.20–2.92 (m, 2H), 1.98 (s, 3H), 1.37 (t, *J* = 7.5 Hz, 3H), 1.32 (t, *J* = 7.5 Hz, 2H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2w***): δ = 11.14 (s, 1H), 7.32–7.23 (m, 2H), 7.22–7.07 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.00–6.98 (m, 2H), 6.94–6.91 (m, 1H), 4.35–4.08 (m, 2H), 2.75 (q, *J* = 7.5 Hz, 2H), 2.18 (s, 3H), 1.38–1.31 (m, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.9, 167.7, 167.2, 166.4, 157.5, 157.0, 152.0, 151.5, 139.4, 134.6, 134.5, 134.3, 133.8, 130.0(2), 129.9, 129.4, 125.7, 125.6, 125.0, 124.9, 123.8, 123.0, 122.9, 120.2, 119.4, 117.9, 117.5, 98.0, 96.7, 59.7, 27.0, 25.3, 17.8, 17.0, 14.3, 14.2, 13.6. HR-MS (ESI): *m/z* = 459.0681, calcd. for $C_{21}H_{22}Cl_2N_2NaO_2S$ $(M+Na)^+$: 459.0671.

Synthesis of *N*-Aryl-Imino *N,S*-Acetals 2 under basic conditions (taking **2a** as an example). To the solution of (*Z*)-ethyl 3-phenyl-3-(phenylamino)acrylate (134 mg, 0.50 mmol) in DMF (3 mL) was added NaH (26 mg, 1.1 mmol). Then, phenyl isothiocyanate (81 mg, 0.6 mmol) was added dropwise to the mixture and stirred for 20 min at room temperature, followed by the addition of bromoethane (65 mg, 0.6 mmol). After the reaction was finished as indicated by TLC (reaction time, 3.0 h), the resulting mixture was poured into saturated aqueous NaCl (20 mL), and extracted with diethyl ether (20 mL× 3). The combined organic phase was dried with anhydrous Na_2SO_4, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel (EtOAc/PE = 1: 60) to afford **2x** (215 mg, 90%).

Ethyl 3-(Ethylthio)-2-(phenyl(phenylimino)methyl)-3-(phenylamino)acrylate(2x) [*E*/*Z*=2:3]: yield: 215 mg (90%); yellowish viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-***2x***): δ = 11.11 (s, 1H), 7.50–6.40 (m, 15H), 4.33–4.26 (m, 2H), 2.95–2.82 (m, 2H), 1.37–1.31 (m, 3H), 1.19–1.10 (m, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-***2x***): δ = 11.30 (s, 1H), 7.50–6.40 (m, 15H), 4.33–4.26 (m, 2H), 2.83–2.76 (m, 2H), 1.37–1.31 (m, 3H), 1.19–1.10 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.4, 168.3, 165.4, 163.4, 159.0, 158.4, 150.3, 149.5, 139.1, 139.0, 133.1, 132.7, 129.2, 129.1(2), 128.6, 128.5, 128.2, 127.9, 127.5, 123.8, 123.5(2), 123.0, 122.9, 122.7, 120.9, 118.8, 99.5, 97.7, 60.0, 59.9, 26.9, 25.2, 14.2(2), 13.8, 13.7. HR-MS (ESI): *m/z* = 431.1787, calcd. for $C_{26}H_{27}N_2O_2S$ $(M+H)^+$: 431.1788.

4-(4-Chlorophenylimino)-3-(ethylthio(4-methoxy phenylamino)methylene)pentan-2-one(2y) [*E*/*Z*=1:3]: yield: 147 mg (73%); yellowish solid; mp 86–87 °C; ^{1}H NMR (500 MHz, $CDCl_3$) (*Z*-***2y***): δ = 13.23 (s, 1H), 7.28 (d, *J* = 8.5 Hz, 2H), 6.94–6.89 (m, 2H), 6.83–6.76 (m, 4H), 3.77 (s, 3H), 3.14–3.03 (m, 2H), 2.21 (s, 3H), 1.95 (s, 3H), 1.39 (t, *J* = 7.0 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) (*E*-***2y***): δ = 13.32 (s, 1H), 7.35 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.94–6.89 (m, 4H), 3.81 (s, 3H), 2.75–2.71 (m, 2H), 2.36 (s, 3H), 2.15 (s, 3H), 1.20 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.0, 193.9, 168.4, 166.0, 159.4, 156.5, 156.1, 143.2, 142.7, 136.4, 131.9, 131.7, 129.3, 129.2, 126.7, 126.5, 121.9, 120.5, 114.2, 113.9, 109.2, 107.8, 55.3, 28.0, 27.8, 27.5, 25.3, 17.7, 17.0, 14.3, 13.8. HR-MS (ESI): *m/z* = 425.1054, calcd. for $C_{21}H_{23}ClN_2NaO_2S$ $(M+Na)^+$: 425.1061.

Ethyl 2-((benzylamino)(ethylthio)methylene)-3-(phenylimino)butanoate(2z) [*E*/*Z*=1:4]: yield: 2.71 g (71%); yellowish viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) (*Z*-***2z***): δ = 11.09 (s, 1H), 7.43–7.11 (m, 8H), 7.07 (d, *J* = 7.6 Hz, 2H), 4.74–4.46 (m, 2H), 4.29–4.04 (m, 2H), 3.07–2.97 (m, 2H), 1.93 (s, 3H), 1.39–1.24 (m, 3H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (*E*-***2z***): δ = 11.10 (s, 1H), 7.43–7.11 (m, 8H), 7.10–7.05 (m, 2H), 4.74–4.46 (m, 2H), 4.29–4.04 (m, 2H), 2.83 (q, *J* = 7.2 Hz, 2H), 2.00 (s, 3H), 1.39–1.24 (m, 3H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.3, 167.4, 164.1, 163.8, 158.7, 158.1, 140.7, 139.7, 138.5, 138.4, 129.0(2), 128.1, 128.0, 127.4, 126.4, 126.2, 125.6, 125.5, 125.2, 125.0, 97.9, 94.7, 59.4(2), 56.7, 56.3, 26.5, 24.4, 17.1, 17.0, 14.6, 14.4, 14.2, 14.1. HR-MS (ESI): *m/z* = 467.1769, calcd. for $C_{27}H_{28}N_2NaO_2S$ $(M+Na)^+$: 467.1764.

(*E*)-Ethyl 3,3-bis(ethylthio)-2-(phenyl(phenylimino) methyl)acrylate(6x): yield: 108 mg (54%); orange solid; mp 53–54 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 7.6, 2H), 7.47–7.37 (m, 3H), 7.29–7.22 (m, 2H), 7.04 (t,

J = 7.6 Hz, 1H), 6.99–6.93 (m, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 2.98–2.49 (m, 4H), 1.14–0.92 (m, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 163.5, 163.4, 151.9, 150.7, 138.3, 131.8, 130.4, 128.2, 128.1, 128.0, 123.8, 119.7, 60.8, 29.4, 29.3, 14.8, 14.6, 13.8. HR-MS (ESI): *m/z* = 422.1213, calcd. for $C_{22}H_{25}NNaO_2S_2$ $(M+Na)^+$: 422.1219.

General procedure for the synthesis of 3 (taking **3a** as an example). To the solution of **2a** (184.0 mg, 0.5 mmol) in toluene (1 mL) was added potassium carbonate (138.2 mg, 1 mmol), anhydrous cupric chloride (6.7 mg, 0.05 mmol), and 1,10-phenanthroline (10 mol%)and stirred at 80 °C. After **2a** was consumed as indicated by TLC (reaction time, 12.0 h), the mixture was poured into saturated aqueous NaCl (30 mL), and extracted with dichloromethane (30 mL × 3), the combined organic phase was dried over anhydrous $Na_2SO_4$and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel (EtOAc/PE/TEA = 20: 120:1) to afford **3a** (127 mg, 83%).

Ethyl 2-methyl-4-(phenylamino)quinoline-3-carboxylate(3a): yield: 127 mg (83%); yellowish solid; mp 114–115 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.66 (s, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.61 (t, *J* = 7.0 Hz, 1H), 7.24–7.18 (m, 3H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 2H), 4.33 (q, *J* = 7.0 Hz, 2H), 2.83 (s, 3H), 1.38 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.7, 157.4, 148.6(2), 143.5, 130.6, 129.0, 128.9, 125.3, 124.5, 122.7, 119.9, 119.7, 113.3, 61.4, 26.3, 13.9. HR-MS (ESI): *m/z* = 307.1449, calcd. for $C_{19}H_{19}N_2O_2$ $(M+H)^+$: 307.1441.

Ethyl 2,6-dimethyl-4-(*p*-tolylamino)quinoline-3-carboxylate(3b): yield: 157 mg (94%); yellow solid; mp 89–90 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.49 (s, 1H), 7.82 (d, *J* = 8.5 Hz, 1H), 7.49 (s, 1H), 7.42 (d, *J* = 8.5 Hz,1H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 4.26 (q, *J* = 7.0 Hz, 2H), 2.78 (s, 3H), 2.27 (s, 3H), 1.34 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.7, 156.2, 148.1, 146.9, 140.7, 134.0, 132.5, 132.2, 129.3, 128.4, 123.8, 120.1, 119.6, 112.7, 61.1, 25.7, 21.3, 20.5, 13.8. HR-MS (ESI): *m/z* = 335.1744, calcd. for $C_{21}H_{23}N_2O_2$ $(M+H)^+$: 335.1754.

Ethyl 2,7-dimethyl-4-(*m*-tolylamino)quinoline-3-carboxylate(3c) and ethyl 2,5-dimethyl-4-(*m*-tolylamino)quinoline-3-carboxylate(3c'): yield: 144 mg (86%); yellowish solid: mp 68–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (***3c***): δ = 8.69 (s, 1H), 7.71 (s, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 7.44–7.00 (m, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.77 (s, 1H), 6.72–6.67 (m, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 2.81 (s, 3H), 2.47 (s, 3H), 2.26 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (***3c'***): δ = 7.83 (d, *J* = 8.4 Hz, 1H), 7.79 (s, 1H), 7.54 (t, *J* = 8.4 Hz, 1H), 7.12–7.08 (m, 1H), 7.04–7.00 (m, 1H), 6.72–6.67 (m, 1H), 6.46 (s, 1H), 6.37 (d, *J* = 8.4 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 2.76 (s, 3H), 2.55 (s, 3H), 2.20 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.0, 168.5, 157.6, 156.2, 150.1, 149.1, 149.0, 147.9, 144.8, 143.6, 141.3, 139.1, 135.5, 130.4, 129.1, 129.0, 128.9, 128.1, 127.3, 126.6, 125.4, 123.6, 122.3, 122.3, 120.8, 118.7, 117.6, 117.5, 117.2, 113.6, 112.4, 61.5, 61.4, 26.6, 25.3, 23.2, 21.7, 21.4(2), 14.1, 13.9. HR-MS (ESI): *m/z* = 335.1744, calcd. for $C_{21}H_{23}N_2O_2$ $(M+H)^+$: 335.1754.

Ethyl 6-methoxy-4-(4-methoxyphenylamino)-2-methyl quinoline-3-carboxylate(3d): yield: 183 mg (89%); yellowish solid; mp 89–90 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.75 (s, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.23 (d, *J* = 9.0 Hz, 1H), 6.93–6.91 (m, 3H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.34 (q, *J* = 7.5 Hz, 2H), 3.76 (s, 3H), 3.45 (s, 3H), 2.78 (s, 3H), 1.39 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.2, 155.9, 155.8, 155.1, 149.0, 144.6, 136.6, 130.3, 123.0, 122.9, 119.8, 114.3, 111.9, 104.2, 61.4, 55.5, 54.9, 26.3, 14.1. HR-MS (ESI): *m/z* = 367.1642, calcd. for $C_{21}H_{23}N_2O_4$ $(M+H)^+$: 367.1652.

Ethyl 6-fluoro-4-(4-fluorophenylamino)-2-methyl quinoline-3-carboxylate(3e): yield: 133 mg (78%); white solid; mp 98–99 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.57 (s, 1H), 7.92 (dd, *J* = 9.0, 5.5 Hz, 1H), 7.38 (ddd, *J* = 9.0, 8.0, 3.0 Hz, 1H), 7.24 (dd, *J* = 10.0, 3.0 Hz, 1H), 6.98–6.94 (m, 2H), 6.89–6.87 (m, 2H), 4.36 (q, *J* = 7.0 Hz, 2H), 2.80 (s, 3H), 1.40 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.7, 159.0 (d, *J* = 255.0 Hz), 159.0 (d, *J* = 251.3 Hz), 156.9 (d, *J* = 2.5 Hz), 148.7 (d, *J* = 5.0 Hz), 145.8, 139.1 (d, *J* = 2.5 Hz), 131.6 (d, *J* = 8.8 Hz), 121.1 (d, *J* = 8.8 Hz), 120.7 (d, *J* = 25 Hz), 120.2 (d, *J* = 8.8 Hz), 116.1 (d, *J* = 22.5 Hz), 113.6, 109.2 (d, *J* = 25.0 Hz), 61.8, 26.3, 14.1. HR-MS (ESI): *m/z* = 343.1245, calcd. for $C_{19}H_{17}F_2N_2O_2$ $(M+H)^+$: 343.1253.

Ethyl 6-chloro-4-(4-chlorophenylamino)-2-methyl quinoline-3-carboxylate(3f): yield: 123 mg (66%); yellowish solid; mp 144–145 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.47 (s, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.63 (s, 1H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 4.32 (q, *J* = 7.0 Hz, 2H), 2.77 (s, 3H), 1.37 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.4, 157.6, 147.0(2), 141.7, 131.6, 130.7(2), 129.2, 127.9, 123.8, 120.7, 114.8, 61.9, 26.1, 14.0. HR-MS (ESI): *m/z* = 375.0655, calcd. for $C_{19}H_{17}Cl_2N_2O_2$ $(M+H)^+$: 375.0662.

Ethyl 6-bromo-4-(4-bromophenylamino)-2-methyl quinoline-3-carboxylate(3g): yield: 187 mg (81%); yellowish solid; mp 124–125 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 7.83 (s, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 4.29 (q, *J* = 7.0 Hz, 2H), 2.75 (s, 3H), 1.36 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 157.7, 147.2, 146.6, 142.1, 134.2, 132.1, 130.8, 126.9, 121.3, 120.9, 118.8, 115.3, 114.9, 61.9, 26.1, 14.0. HR-MS (ESI): *m/z* = 462.9640, calcd. for $C_{19}H_{17}Br_2N_2O_2$ $(M+H)^+$: 462.9651.

Ethyl 6-iodo-4-(4-iodophenylamino)-2-methylquinoline-3-carboxylate(3h): yield: 201 mg (72%); white solid; mp 156–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (s, 1H), 8.05 (s, 1H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 8.8 Hz, 2H), 6.64 (d, *J* = 8.8 Hz, 2H), 4.32 (q, *J* = 7.2 Hz, 2H), 2.77 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 158.1, 147.7, 146.6, 142.9, 139.6, 138.1, 133.9, 130.9, 121.8, 121.4, 114.9, 90.1, 85.6, 61.9, 26.3, 14.1. HR-MS (ESI): *m/z* = 558.9377, calcd. for $C_{19}H_{17}I_2N_2O_2$ $(M+H)^+$: 558.9374.

Ethyl 7-methoxy-4-(3-methoxyphenylamino)-2-methyl quinoline-3-carboxylate(3i) and ethyl 5-methoxy-4-(3-methoxyphenylamino)-2-methylquinoline-3-carboxylate(3i'): yield: 146 mg (80%); yellowish solid; mp 83–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) (***3i***): δ = 8.83 (s, 1H), 7.63 (d, *J* = 9.2 Hz, 1H), 7.55–7.51 (m, 1H), 7.25 (s, 1H), 7.11 (t, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 9.2 Hz, 1H), 6.51–6.47 (m, 1H), 6.45 (s, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 3H), 3.69 (s, 3H), 2.82 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) (***3i'***): δ = 9.50 (s, 1H), 7.56–7.50 (m, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 6.8 Hz, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 6.69 (s, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.45 (s, 1H), 3.98 (s, 3H), 3.78 (s, 3H), 3.62 (q, *J* = 7.2 Hz, 2H), 2.63 (s, 3H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.0, 168.2, 161.8, 160.4, 160.2, 158.4, 157.7, 157.0, 150.9, 149.2, 148.5, 145.0, 142.4, 129.9, 129.8(2), 127.2, 122.2, 117.3, 114.3, 114.2, 112.5, 111.6, 111.1, 110.4, 110.2, 108.4, 107.1, 105.8, 104.8, 61.5, 60.7, 56.4, 55.5, 55.2(2), 26.7, 24.6, 14.1, 13.8. HR-MS (ESI): *m/z* = 367.1658, calcd. for $C_{21}H_{23}N_2O_4$ $(M+H)^+$: 367.1652.

Ethyl 4-(biphenyl-4-ylamino)-2-methyl-6-phenylquinoline-3-carboxylate(3j): yield: 211 mg (92%); yellowish solid; mp 132–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.05 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.91–7.86 (m, 2H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H),

7.27–7.23 (m, 5H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.38 (q, *J* = 7.2 Hz, 2H), 2.86 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ=168.8, 157.5, 149.1, 148.0, 142.7, 140.3, 139.8, 136.7, 136.1, 130.0, 129.3, 128.7, 128.6, 127.7, 127.2, 126.9(2), 126.5, 123.6, 121.0, 119.3, 112.5, 61.4, 26.5, 14.0. HR-MS (ESI): *m/z* = 459.2053, calcd. for $C_{31}H_{27}N_2O_2$ $(M+H)^+$: 459.2067.

Ethyl 2,8-dimethyl-4-(*o*-tolylamino)quinoline-3-carboxylate(3k): yield: 149 mg (89%); yellowish solid; mp 91–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (s, 1H), 7.47–7.43 (m, 2H), 7.21 (t, *J* = 4.8 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.95–6.93 (m, 2H), 6.60 (t, *J* = 4.8 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 2.84 (s, 3H), 2.76 (s, 3H), 2.41 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.1, 156.2, 149.7, 147.7, 142.4, 136.9, 130.8, 130.6, 128.7, 126.3, 124.1, 123.2, 122.9, 120.0, 119.6, 112.8, 61.4, 26.9, 18.2, 18.1, 14.0. HR-MS (ESI): *m/z* = 335.1748, calcd. for $C_{21}H_{23}N_2O_2$ $(M+H)^+$: 335.1754.

Ethyl 2-methyl-6-(trifluoromethyl)-4-(4-(trifluoromethyl)phenylamino)quinoline-3-carboxylate (3l): yield: 166 mg (75%); white solid; mp 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 (s, 1H), 8.06 (d, *J* = 8.8 Hz, 1H), 8.00 (s, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.84 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 160.0, 149.9, 147.9, 146.2, 130.5, 127.2 (q, *J* = 32.5 Hz), 126.7 (q, *J* = 2.6 Hz), 126.6 (q, *J* = 3.6 Hz), 123.1 (q, *J* = 4.5 Hz), 119.4, 118.7, 116.1, 62.2, 26.4, 14.0. ^{19}F NMR (470 MHz, $CDCl_3$): δ = -64.0, -64.5. HR-MS (ESI): *m/z* = 443.1178, calcd. for $C_{21}H_{17}F_6N_2O_2$ $(M+H)^+$: 443.1189.

1-(2-Methyl-4-(phenylamino)quinolin-3-yl)ethanone (3m): yield: 169 mg (71%); white solid; mp 137–138 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.64 (t, *J* = 6.8 Hz, 1H), 7.54 (s, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 2H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 2H), 2.72 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.9, 155.2, 148.6, 144.2, 143.6, 130.5, 129.3, 129.0, 125.2, 124.4, 122.3, 120.9, 118.6, 32.0, 25.0. HR-MS (ESI): *m/z* = 277.1331, calcd. for $C_{18}H_{17}N_2O$ $(M+H)^+$: 277.1335.

1-(2,6-Dimethyl-4-(*p*-tolylamino)quinolin-3-yl)ethanone (3n): yield: 137 mg (90%); white solid; mp 136–137 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.4 Hz, 1H), 7.56 (s, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.33 (s, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 8.0 Hz, 2H), 2.67 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.9, 154.3, 147.1, 144.1, 140.9, 135.1, 132.6, 132.0, 129.7, 128.8, 124.7, 122.8(2), 119.1, 31.9, 24.8, 21.7, 20.7. HR-MS (ESI): *m/z* = 305.1658, calcd. for $C_{20}H_{21}N_2O$ $(M+H)^+$: 305.1648.

1-(6-Methoxy-4-(4-methoxyphenylamino)-2-methyl quinolin-3-yl)ethanone(3o): yield: 160 mg (95%); white solid; mp 120–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (s, 1H), 7.82 (d, *J* = 8.8 Hz, 1H), 7.25 (d, *J* = 8.8 Hz, 1H), 7.02 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 3.75 (s, 3H), 3.52 (s, 3H), 2.66 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.0, 156.3, 155.5, 152.6, 144.6, 144.4, 136.5, 130.3, 123.6, 122.6, 121.8, 120.9, 114.4, 102.9, 55.4, 55.0, 32.0, 24.8. HR-MS (ESI): *m/z* = 337.1548, calcd. for $C_{20}H_{21}N_2O_3$ $(M+H)^+$: 337.1547.

1-(6-Fluoro-4-(4-fluorophenylamino)-2-methylquinolin-3-yl)ethanone(3p): yield: 117 mg (75%); white solid; mp 145–146 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (dd, *J* = 9.0, 5.5 Hz, 1H), 7.52 (s, 1H), 7.40 (ddd, *J* = 9.0, 8.0, 3.0 Hz, 1H), 7.30 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.96–6.92 (m, 2H), 6.83–6.79 (m, 2H), 2.69 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.8, 159.5 (d, *J* = 245.9 Hz), 158.6 (d, *J* = 241.0 Hz), 154.5 (d, *J* = 2.6 Hz), 145.7, 144.1 (d, *J* = 5.0 Hz), 139.2 (d, *J* = 2.6 Hz), 131.6 (d, *J* = 8.8 Hz), 125.5, 121.4 (d, *J* = 9.3 Hz), 120.6 (d, *J* = 12.5 Hz), 120.4, 116.1 (d, *J* = 22.6 Hz), 108.1 (d, *J* = 23.8 Hz), 32.0, 24.8. HR-MS (ESI): *m/z* = 313.1143, calcd. for $C_{18}H_{15}F_2N_2O$ $(M+H)^+$: 313.1147.

1-(6-Chloro-4-(4-chlorophenylamino)-2-methylquinolin-3-yl)ethanone(3q): yield: 124 mg (72%); white solid; mp 171–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.8 Hz, 1H), 7.69 (s, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.28 (s, 1H), 7.19 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 8.8 Hz, 2H), 2.70 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.5, 155.5, 147.1, 142.7, 141.9, 131.6, 131.5, 130.9, 129.5, 127.5, 126.8, 123.1, 121.9, 119.4, 31.9, 24.9. HR-MS (ESI): *m/z* = 345.0552, calcd. for $C_{18}H_{15}Cl_2N_2O$ $(M+H)^+$: 345.0556.

1-(6-Bromo-4-(4-bromophenylamino)-2-methylquinolin-3-yl)ethanone(3r): yield: 171 mg (79%); white solid; mp 177–178 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (s, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.21 (s, 1H), 6.69 (d, *J* = 8.8 Hz, 2H), 2.69 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.5, 155.7, 147.3, 142.5, 142.4, 134.1, 132.4, 131.0, 126.9, 126.4, 122.4, 119.7(2), 114.9, 32.0, 24.9. HR-MS (ESI): *m/z* = 432.9545, calcd. for $C_{18}H_{15}Br_2N_2O$ $(M+H)^+$: 432.9546.

1-(4-(Biphenyl-4-ylamino)-2-methyl-6-phenylquinolin-3-yl)ethanone(3s): yield: 171 mg (80%); yellow solid; mp 188–190 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 9.0 Hz, 1H), 7.96–7.95 (m, 2H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.56 (d, *J* = 7.0 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.36–7.24 (m, 6H), 6.98 (d, *J* = 8.0 Hz, 2H), 2.76 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.8, 155.4, 148.1, 144.9, 142.9, 140.4, 140.0, 137.7, 135.7, 130.1, 129.5, 128.8(2), 128.0, 127.5, 127.2, 127.0, 126.6, 124.9, 122.8, 120.6, 119.8, 32.2, 25.4. HR-MS (ESI): *m/z* = 429.1955, calcd. for $C_{30}H_{25}N_2O$ $(M+H)^+$: 429.1961.

1-(2-Methyl-6-(trifluoromethyl)-4-(4-(trifluoromethyl) phenylamino)quinolin-3-yl)ethanone(3t): yield: 144 mg (70%); white solid; mp 192–193 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 9.0 Hz, 1H), 8.02 (s, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.45 (s, 1H), 6.85 (d, *J* = 8.5 Hz, 2H), 2.76 (s, 3H), 2.52 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.3, 157.7, 149.8, 146.3, 143.2, 130.6, 128.4, 127.8 (q, *J* = 32.5 Hz), 126.9 (q, *J* = 3.6 Hz), 126.5 (q, *J* = 3.3 Hz), 122.2 (q, *J* = 4.8 Hz), 120.7, 117.1, 31.9, 25.0. ^{19}F NMR (470 MHz, $CDCl_3$): δ = -63.9, -64.5. HR-MS (ESI): *m/z* = 413.1078, calcd. for $C_{20}H_{15}F_6N_2O(M+H)^+$: 413.1083.

Ethyl 2-methyl-4-(naphthalen-1-ylamino)benzo[*h*] quinoline-3-carboxylate(3u): yield: 201 mg (99%); yellowish solid; mp 115–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.33 (d, *J* = 8.0 Hz, 1H), 9.08 (s, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.73–7.51 (m, 6H), 7.43 (d, *J* = 9.2 Hz, 1H), 7.32 (d, *J* = 9.2 Hz, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 2.99 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.1, 157.0, 149.8, 147.3, 140.2, 134.4, 133.9, 131.2, 128.6, 128.4, 127.4, 126.9, 126.7, 126.5, 126.3, 125.6, 125.3, 125.2, 123.1, 122.3, 121.6, 117.0, 115.7, 114.8, 61.6, 26.9, 14.0. HR-MS (ESI): *m/z* = 407.1744, calcd. for $C_{27}H_{23}N_2O_2$ $(M+H)^+$ 407.1754.

1-(2-Methyl-4-(naphthalen-1-ylamino)benzo[*h*]quinolin-3-yl)ethanone(3v): yield: 184 mg (98%); yellowish solid; mp 184–185 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.27 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 9.2 Hz, 1H), 8.02 (s, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.66–7.41 (m, 7H), 7.30 (d, *J* = 9.2 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 2.82 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.0, 154.1, 147.0, 145.3, 140.2, 134.3, 133.7, 131.1, 128.5, 128.4, 127.4, 126.8, 126.6, 126.4, 126.2, 126.0, 125.6, 124.9, 122.7, 121.4, 121.2, 118.1, 114.5, 31.9, 25.5. HR-MS (ESI): *m/z* = 377.1638, calcd. for $C_{26}H_{21}N_2O$ $(M+H)^+$: 377.1648.

Ethyl 7-chloro-4-(3-chlorophenylamino)-2-methyl quinoline-3-carboxylate(3w): yield: 118 mg (63%); yellowish solid; mp 108–109 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.65 (s, 1H), 7.93 (s, 1H), 7.60 (d, *J* = 9.0 Hz, 1H), 7.18 (d, *J* = 9.0 Hz, 1H), 7.13 (t, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.88 (s, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 4.37 (q, *J* = 7.5 Hz, 2H), 2.80 (s, 3H), 1.40 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.4, 158.9, 149.3, 148.0, 144.7, 136.9, 135.0, 130.2, 128.2, 126.6, 125.9, 122.9, 119.6, 118.3, 117.7, 114.3, 61.9, 26.4, 14.0. HR-MS (ESI): *m/z* = 375.0654, calcd. for $C_{19}H_{17}Cl_2N_2O_2$ $(M+H)^+$: 375.0662.

Ethyl 2-phenyl-4-(phenylamino)quinoline-3-carboxylate(3x): yield: 169 mg (92%); white solid; mp 141–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (s, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.66–7.61 (m, 3H), 7.46–7.39 (m, 3H), 7.24–7.19 (m, 3H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 2H), 3.93 (q, *J* = 7.2 Hz, 2H), 0.73 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.3, 158.9, 148.9, 148.5, 143.5, 142.2, 130.8, 130.1, 129.1, 128.1, 128.0, 125.9, 124.9, 123.0, 120.2, 119.5, 113.7, 61.3, 13.0. HR-MS (ESI): *m/z* = 369.1607, calcd. for $C_{24}H_{20}N_2O_2$ $(M+H)^+$: 369.1598.

Ethyl 2-phenyl-4-(phenylamino)quinoline-3-carboxylate(3x): yield: 169 mg (92%); white solid; mp 141–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (s, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.66–7.61 (m, 3H), 7.46–7.39 (m, 3H), 7.24–7.19 (m, 3H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 2H), 3.93 (q, *J* = 7.2 Hz, 2H), 0.73 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.3, 158.9, 148.9, 148.5, 143.5, 142.2, 130.8, 130.1, 129.1, 128.1, 128.0, 125.9, 124.9, 123.0, 120.2, 119.5, 113.7, 61.3, 13.0. HR-MS (ESI): *m/z* = 369.1607, calcd. for $C_{24}H_{20}N_2O_2$ $(M+H)^+$: 369.1598.

1-(6-Chloro-4-(4-methoxyphenylamino)-2-methyl quinolin-3-yl)ethanone(3y): yield: 161 mg (87%); white solid; mp 165–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 9.2 Hz, 1H), 7.76 (s, 1H), 7.75 (s, 1H), 7.52 (d, *J* = 9.2 Hz, 1H), 6.88 (d, *J* = 9.2 Hz, 2H), 6.79 (d, *J* = 9.2 Hz, 2H), 3.77 (s, 3H), 2.65 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.5, 156.1, 155.8, 146.9, 145.0, 135.7, 131.0, 130.6, 130.5, 123.1, 122.9, 122.3, 121.0, 114.6, 55.4, 31.9, 24.9. HR-MS (ESI): *m/z* = 341.1051, calcd. for $C_{19}H_{18}ClN_2O_2$ $(M+H)^+$: 341.1043.

Ethyl 4-(benzylamino)-2-methylquinoline-3-carboxylate (3z): yield: 40 mg (25%); orange viscous liquid; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.39–7.30 (m, 6H), 6.87 (s, 1H), 4.67 (d, *J* = 5.4 Hz, 2H), 4.33 (q, *J* = 7.2 Hz, 2H), 2.72 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.6, 157.3, 152.8, 148.4, 138.5, 130.5, 129.0, 128.9, 127.8, 127.5, 124.4, 123.1, 118.7, 108.6, 61.3, 52.2, 25.9, 14.0. HR-MS (ESI): *m/z* = 321.1590, calcd. for $C_{20}H_{21}N_2O_2$ $(M+H)^+$: 321.1598.

***N*-((cyclohexylimino)methylene)aniline(10):** yield: 69 mg (69%); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27 (t, *J* = 7.6 Hz, 2H), 7.13 – 7.04 (m, 3H), 3.46 (m, 1H), 2.14 – 1.90 (m, 2H), 1.81 – 1.71 (m, 2H), 1.62 – 1.41 (m, 3H), 1.40 – 1.18 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 140.9, 136.1, 129.2, 124.4, 123.3, 56.5, 34.9, 25.3, 24.3.

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FULL PAPER

Cu(II)-Catalyzed Desulfitative 6π Electrocyclization: Efficient Synthesis of Diverse 4-Aminoquinolines

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Lou Shi, Ling Pan,* Yifei Li and Qun Liu*