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Metal-Free Oxidative *para*-Acylation of Unprotected Anilines with *N*-Heteroarylmethanes

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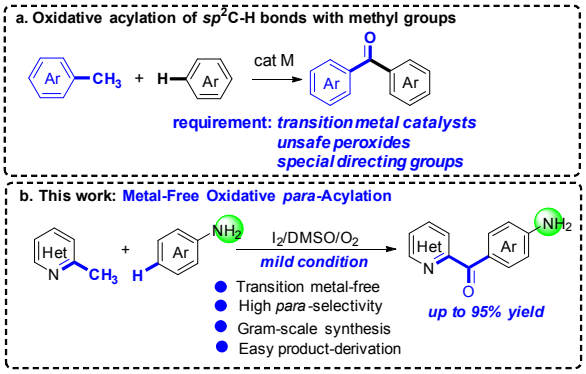
A selective oxidative *para*-acylation of unprotected anilines with methyl group in *N*-heteroarylmethanes was achieved. This transformation proceeds under a mild metal-free reaction conditions to produce the corresponding valuable diarylmethanones in good to high yields, featuring high site-selectivity, high functional-group-tolerance, gram-scale synthesis and easy product-derivation. Preliminary mechanistic studies revealed that the present oxidative *para*-acylation would take place *via* a Friedel-Crafts-type process of *in-situ* imines and the steric hindrance might be the key issue for the high *regio*-selectivity.

Introduction

Selective C-H functionalization is a continuing challenge in organic synthesis.[1] One of the specifically active fields utilizes the reactions between two hydrocarbons to construct functional molecules. This strategy is usually achieved by transition metal catalysis.[2] Despite it serves well for constructing chemical bonds, the concomitant metal contamination of the products as well as the high price of metal catalysts makes its application difficult in development of bioactive reagents and organic electronic devices.[3] Recently, the transition metal-free cross coupling between different C-H bonds is recognized to be a green alternative and attracts much attention, however, it remains challengeable.[4]

Diarylmethanones commonly occur as key units in a variety of natural products, chemical drugs and material molecules.[5] They are also an important kind of building blocks in organic synthesis.[6] Conventional procedures for their synthesis are highly dependent on the transformation of reactive functional groups. For example, the cross couplings between acyl halides and aryl metals can produce diarylmethanones.[7] The tandem strategy involving Friedel-Crafts reaction of trihalomethylbenzenes with electron-rich aromatics and subsequent hydrolysis is also extensively used, despite usually suffering from *regio*-selective issues.[8] The oxidation of diarylmethanes[9] and transition metal-catalyzed carbonylative Suzuki couplings of aryl borons[10] are also developed for the synthesis of such compounds. Recently, the oxidative site-selective acylation of sp^2C-H bonds with methyl groups is achieved (Scheme 1a).[11] This transformation would be the most straightforward protocol for preparing diarylmethanones because of the high step- and atom-economic efficiency; however, transition metal catalysts, unsafe peroxides and/or special directing groups are required, leading to issues of low synthetic efficiency and metal contamination of products. We envisioned that if the oxidative acylation of sp^2C-H bonds with sp^3C-H bond of *N*-heteroarylmethanes could take place *regio*-selectively under metal-free reaction conditions using dioxygen molecules as an oxidant, it would be highly appreciated for the green synthesis of diarylmethanones. Herein, we communicated a selective oxidative *para*-acylation of unprotected anilines with methyl groups in *N*-heteroaryl methanes to selectively generate the value-added (4-aminophenyl)arylmethanones under such a mild reaction condition (Scheme 1b). Mechanistic studies showed that this reaction proceeded *via* a Friedel-Crafts-type process of *in-situ* imines, in which a strong steric effect ensured the high *para*-selectivity of the oxidative acylation.



Scheme 1 Preparation of diarylmethanones.

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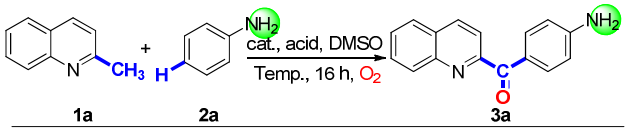
Results and discussion

Discovery of the oxidative *para*-acylation. In 2016, we reported a facile I_2/DMSO/O_2 system which enables the oxidative *ortho*-acylation of phenols with *N*-heteroarylmethanes to *regio*-selectively produce the corresponding (2-hydroxyphenyl)arylmethanones in moderate yields.[12] The site-selectivity is deduced to be controlled by the *in-situ* hydrogen bonds. Regarding to the similarity of structures, aniline was used instead of phenols under the reaction conditions. To our surprise, the *para*-C-H bond rather than the *ortho*-C-H bond was oxidatively acylated selectively and the product (4-aminophenyl)(quinolin-2-yl)methanone was produced in ca. 20% yield.

Table 1 Direct oxidative acylation of aniline with 2-methylquinoline[a]



1a 2a 3a

Entry	Cat. [mol%]	Acid (20 mol%)	Temp. [°C]	Yield [%][b]
1	I_2	-	60	74
2	I_2	salicylic acid	60	93
3[c]	I_2	salicylic acid	60	90
4	I_2	PhC(O)OH	60	89
5	I_2	$CF_3C(O)OH$	60	87
6	I_2	*p*-TsOH	60	80
7	I_2	AcOH	60	84
8	I_2	PhOH	60	80
9[d]	I_2	salicylic acid	60	70
10	-	salicylic acid	60	N.D.
11	NaI	salicylic acid	60	80
12	KI	salicylic acid	60	83
13	I_2	salicylic acid	40	46
14	I_2	salicylic acid	80	93
15	I_2	salicylic acid	100	71
16[e]	I_2	salicylic acid	60	35
17[f]	I_2	salicylic acid	60	trace
18[g]	I_2	salicylic acid	60	30
19[h]	I_2	salicylic acid	60	87

[a] A mixture of **1a** (0.2 mmol), **2a** (0.6 mmol), I_2 (0.04 mmol), acid (0.04 mmol) in DMSO (0.2 mL) was heated at 60 °C for 16 h under O_2 atmosphere (1 atm, 25 mL glass tube). [b] GC yield using tridecane as an internal standard. [c] 0.02 mmol acid was loaded. [d] 0.02 mol I_2 was used. [e] under air atmosphere. [f] under N_2 atmosphere. [g] 0.2 mmol **2a** was used. [h] 0.4 mmol **2a** was used. N.D. = Not Detected.

Inspired by the interesting feedback, we further optimized the reaction conditions and the results obtained were compiled in Table 1. After a comprehensive condition screening, it was found that this transformation could proceed efficiently under a milder reaction condition (close to neutral condition). Heating the mixture of 2-methylquinoline, aniline and 20 mol% I_2 in DMSO at 60 °C for 16 h under an atmospheric pressure of dioxygen molecules, **3a** was generated in 74% yield (Table 1, entry 1). By addition of 20 mol% salicylic acid, the yield was increased to 93% (Table 1, entry 2). Further raising the loading of salicylic acid to 40 mol% gave a similar yield (Table 1, entry 3). Other acids like phenol, AcOH, PhC(O)OH, $CF_3C(O)OH$ and TsOH also showed a positive effect on the oxidative acylation (Table 1, entries 4-8).[13] Only 70% yield of **3a** was afforded with 10 mol% loading of I_2 under similar reaction conditions; whereas, no reaction was observed in the absence of iodine (Table 1, entries 9 and 10), indicating that the iodine was essential to this reaction. Other iodines such as NaI and KI could also promote the oxidative *para*-acylation, despite with slightly lower yields (Table 1, entries 11 and 12). Debasing the temperature to 40 °C lead to a dramatic decrease of the yield with the starting material **1a** being retained (Table 1, entry 13). While the reaction was performed at 80 °C, 93% yield of **3a** was provided (Table 1, entry 14) just like that at 60 °C. Further elevating the temperature to 100 °C resulted in a reduced production of **3a**, probably due to the decomposition of quinoline fragment under the reaction conditions (Table 1, entry 15). The reaction could also proceed under an air atmosphere (Table 1, entry 16); however, in the absence of dioxygen, only a trace amount of product could be detected (Table 1, entry 17). Excessive anilines were necessary aiming to obtain a high yield of **3a** (Table 1, entries 18 and 19).[14] When 2 equiv. anilines were loaded, 87% yield of **3a** was generated; while only 30% yield was obtained with 1 equiv. anilines. It should be noted that 90% (0.36 mmol) excess of anilines in entry 2 of Table 1 were detected after reaction by GC using tridecane as an internal standard, indicating that the excessive anilines remained almost intact during the reaction and would be easily reused.

Scope of the methodology. With the optimal reaction conditions in hand, the substrate scope was subsequently investigated. As shown in Table 2, a variety of *N*-heteroarylmethanes oxidatively coupled with anilines, producing the corresponding (4-aminophenyl)arylmethanones in good to excellent yields. Thus, 2-methyl quinolines bearing 6-methyl and 6-methoxy groups reacted with **2a** readily, giving the expected products in high yields (**3b** and **3c**). The halo groups like F, Cl and Br survived well under the reaction conditions, facilitating further functionalization of products *via* cross coupling (**3d**-**3g**). The ester group substituted substrate also showed good reactivity, furnishing the desired product **3h** in 65% yield. 4-Methyl quinoline, 1-methyl isoquinolines and 2-methyl quinoxaline underwent oxidative *para*-acylation with **2a** smoothly under similar reaction conditions; the corresponding products **3i**, **3k** and **3l** were afforded in 95%, 81% and 85% yields, respectively. However, when 3-methyl quinoline was employed as a substrate, no reaction was observed even at a high temperature (**3j**). By elevating the temperature to 110 °C, 4-methylpyridine also oxidatively coupled with **2a** to give **3m** in 90% yield; whereas 2-methylpyridine exhibited low reaction efficiency under similar reaction conditions (**3n**). Benzothiazole derivatives were also found as reactive as quinolines to produce the corresponding products in excellent yields (**3o**-**3q**). The results obtained here are consistent with those of deuteration at the methyl groups of *N*-heteroarylmethanes,[13] in which 1) both 2-methyl and 4-methyl groups were deuterated, 2) 3-methyl group remained intact, and 3) 4-methylpyridine showed higher reactivity than 2-methylpyridine. Thus, a similar activation of methyl groups would be involved in the present oxidative *para*-acylation reactions.

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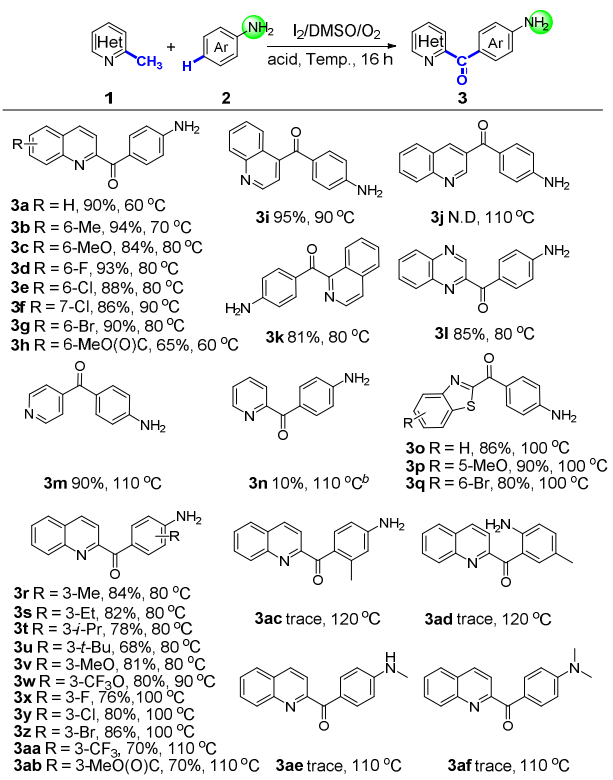
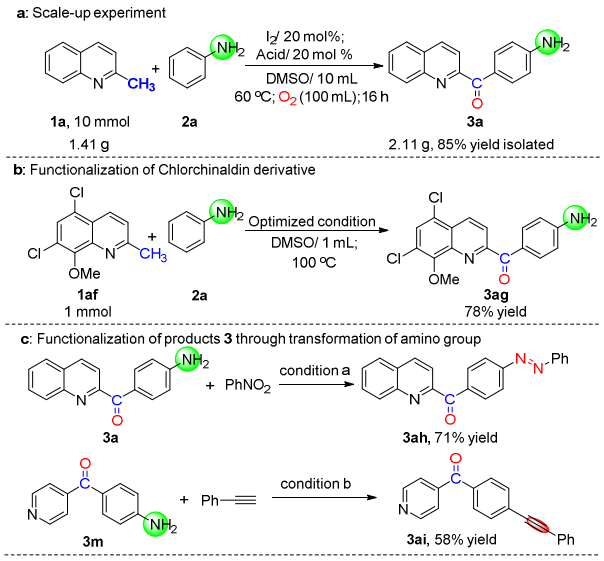
Table 2 Metal-free direct oxidative *para*-acylation of anilines with *N*-heteroarylmethanes[a]



[a] A mixture of **1** (0.2 mmol), **2** (0.6 mmol), I_2 (0.04 mmol), salicylic acid (0.04 mmol) in DMSO (0.2 mL) was heated at the indicated temperature for 16 h under O_2 atmosphere (1 atm, 25 mL glass tube), isolated yield. [b] GC yield using tridecane as an internal standard.

As for the anilines, both electron-rich and electron-deficient 2-substituted derivatives served well in the current catalytic system. Thus, the substrates with 2-methyl, 2-ethyl, 2-isopropyl and 2-*tert*-butyl groups were converted to the corresponding products in good to high yields. It should be noted that the yields seemed to decrease with increase of the steric hindrance of substituent groups (**3a**, **3r**-**3u**). Methoxy and the easily hydrolytic CF_3O groups were compatible to this reaction (**3v** and **3w**). Halo groups like F, Cl and Br also survived (**3x**-**3z**). Anilines having electron-withdrawing groups (CF_3 and ester groups) were also oxidatively *para*-acylated, though a high temperature was required (**3aa** and **3ab**). When *m*-toluidine was employed as a substrate, only a trace amount of product **3ac** was detected, indicating that a strong steric effect existed in this reaction. As described below, this reaction would be a Friedel-Crafts-type process; the oxidative acylation might take place at the *ortho*-position of aniline when its *para*-site is occupied. Therefore, *p*-toluidine was tested; however the reaction proceeded sluggishly (**3ad**). The result perhaps was ascribed to the steric hindrance of amino group. Those results compiled above also implied that the steric effect might contribute to the high *regio*-selectiviy in the present oxidative *para*-acylation of anilines with methyl groups. After the free amino group was methylated or double methylated, the reactions also hardly occurred in the current catalytic system (**3ae** and **3af**).[14]

Demonstration of Synthetic Value of the Reaction. Practically, this reaction could be conducted in a gram-scale, affording the desired product in 85% yield (Scheme 2a, for detailed procedure, see experimental section). Worth noting is that the present oxidative *para*-acylation strategy was applicable to the derivation of bioactive molecules, i.e. chloroxine derivative 5,7-dichloro-8-methoxy-2-methylquinoline coupled readily with **2a** under similar reaction conditions, producing the corresponding diarylmethanone **3ag** in 78% yield (Scheme 2b). The synthetic value of this new reaction was further demonstrated by complexity of the resulting products through transformation of the free amino group (Scheme 2c).[15] For instance, **3a** reacted with nitrobenzene, generating an azo compound **3ah**.[15a] **3m** coupled with phenylacetylene and was converted to an internal alkyne **3ai**.[15b]



Scheme 2 Demonstration of synthetic value of this new reaction. Condition a: **3a** (3 equiv.), $PhNO_2$ (0.5 mmol), KOH (5 equiv.), DMF (3 mL), 150 °C, 24 h. Condition b: **3m** (1.3 equiv.), phenylacetylene (0.4 mmol), $Pd(OAc)_2$ (5 mol%), tri(furan-2-yl)phosphane (15 mol%), *t*-BuONO (1.3 equiv.), AcOH (1.3 equiv.), DMSO (1 mL), 35 °C, N_2, 16 h.

Mechanistic Studies. To gain some mechanistic information on the oxidative *para*-acylation, several control experiments were performed. In the presence of excess radical scavenger TEMPO (2,2,6,6-tetramethylpiperidinyloxy) or BHT (butylated hydroxytoluene), the oxidative *para*-acylation of **2a** with **1a** still took place, indicating that this reaction would be a Friedel-Crafts-type process rather than a radical process (eqn 1). Under the standard reaction conditions, 2-(iodomethyl)quinoline **5a** coupled with anilines to produce **3a** in 75% yield (eqn 2). According to the Kornblum oxidation, aldehyde **6a** could be easily formed from the reaction of **5a** with DMSO in the presence of a base (In this case, excess aniline present in the reaction mixture may play such a role). Thus, **6a** was tested. It was found that **6a** showed high reactivity in the reaction with anilines to produced **3a** in

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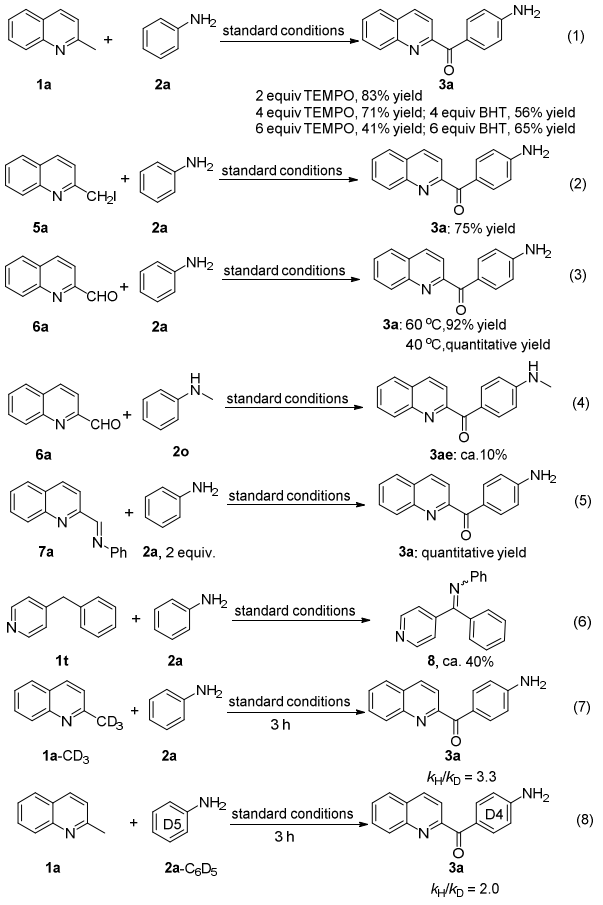
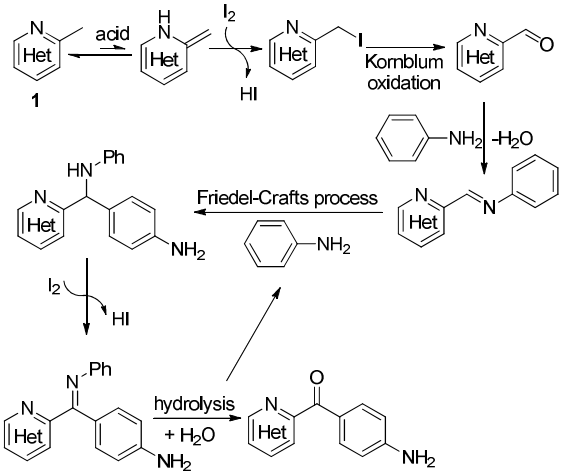
excellent yields even at 40 °C (eqn 3); however, the reaction of **6a** with *N*-Me-anilines **2o** proceeded sluggishly under the reaction conditions (eqn 4).[14] It was known that the aldehyde would react with anilines to generate imines. Thus, it was deduced that an *in-situ* imines would be formed and acted as an active intermediate in this reaction. Indeed, when **7a** was allowed to react with 2 equiv. anilines under the standard reaction conditions, a quantitative **3a** was afforded (eqn 5). The hypothesis was further supported by the experiment: the reaction of 4-benzylpyridine **1t** with anilines took place readily to produce *N*-(phenyl(pyridin-4-yl)methylene)aniline chemo-selectively in ca. 40% yield in the current catalytic system (eqn 6). These results were well associated with experimental phenomenon: 1) Imines were an efficient intermediate, therefore *N*-methyl-aniline and *N*,*N*-dimethyl-aniline were ineffective;[14] 2) because of the high steric hindrance of imines, this reaction showed high steric effect, thus ensuring high *para*-selectivity. Kinetic isotope effect (KIE) experiments were also performed and two kinetic isotope effects were obtained. For **1a**-CD_3, k_H/k_D = 3.3 (eqn 7); when **2a**-C_6D_5 was tested, k_H/k_D = 2.0 (eqn 8), implying that both the C-H bonds in methyl group of *N*-heteroarylmethanes and the *para*-C-H bond in anilines would play an important role in this reaction.



Thus, on the basis of these results described above and previous literatures, a plausible mechanism involving a Friedel-Crafts-type process is proposed in Scheme 3.[16] At first, *N*-heteroarylmethane underwent enamine isomerization,[13] followed by iodination with I_2 to produce a benzylic iodide. The benzylic iodide was then converted to aldehyde in the presence of base *via* Kornblum oxidation, which was captured by an aniline at once, furnishing an active imine intermediate.[14] Subsequently, the imine coupled with another aniline through Friedel-Crafts-type process,[17] giving a secondary amine. After dehydrogenation by I_2 and hydrolysis, the product **3** was produced.[18] During the reaction, I_2 was regenerated from iodo ions by DMSO and O_2 to complete the catalytic cycle.[19]



Scheme 3 Proposed mechanism for the metal-free oxidative acylation.

Conclusions

In summary, we have disclosed an oxidative *para*-acylation of unprotected anilines with *N*-heteroarylmethanes under a mild metal-free reaction condition *via* sp^3C-H and sp^2C-H dual activation. The reaction proceeded in a facile I_2/DMSO/O_2 catalytic system, highly *regio*-selectively producing the corresponding (4-aminophenyl)arylmethanones in good to excellent yields. The high site-selectivity, broad functional-group-compatibility, scale-up experiment, and easy derivation of products **3** through transformation of free amino group clearly demonstrated the potential synthetic value of this new reaction.

Acknowledgements

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Experimental Section

A typical procedure: An oven-dried Schlenk tube containing a stir bar was charged with I_2 (0.04 mmol) and salicylic acid (0.04

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mmol), then degassed and refilled with O_2 for 3 times. After addition of 0.2 mL DMSO, **1a** (0.2 mmol) and **2a** (0.6 mmol) under O_2 atmosphere, the mixture was stirred at 60 °C for 16 h. After dilution with 3-5 mL DCE and subsequent removal of the volatiles, the residues were passed through a short silica chromatography column (particle size 37–54 μm, petroleum ether/ethyl acetate/NEt_3 as eluent) to afford analytically pure **3a** in 90% isolated yield.

Gram-scale *para*-acylation.: An oven-dried 100 mL Schlenk tube containing a stir bar was charged with I_2 (2 mmol, 508 mg), salicylic acid (2 mmol, 280 mg), and degassed and refilled with O_2 for 3 times. After addition of 10 mL DMSO, **1a** 2-methylquinoline (10 mmol, 1.35 mL) and **2a** aniline (30 mmol, 2.7 mL) under O_2 atmosphere, the mixture was stirred at 60 °C for 16 h. During the reaction, O_2 was refilled at 5 h, 10 h. After reaction, the mixture was washed with saturated $NaHCO_3$ aqueous and extracted with DCM. Then the organic layer was evaporated and the residues were passed through a short silica chromatography column (particle size 37–54 μm, petroleum ether/ethyl acetate/NEt_3 as eluent) to afford analytically pure product **3a** (2.11 g, 85% yield).

Characterized Data of the Products

*(4-aminophenyl)(quinolin-2-yl)methanone (**3a**)*. Following the typical procedure (60 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3a** (90% yield, 22.3 mg, Yellow solid, m.p. 163.5-164.2 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.55 (d, *J* = 8.4 Hz, 1H), 8.10 (t, *J* = 9.0 Hz, 2H), 7.86-7.88 (m, 4H), 7.73 (t, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 2H), 6.31 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 191.16, 157.19, 154.77, 146.43, 137.70, 134.02, 130.77, 129.97, 128.51, 128.46, 128.36, 123.31, 120.98, 112.97. HRMS (EI) m/z: [M] Calcd for $C_{16}H_{12}N_2O$ 248.0950, Found 249.1022 (M+H).

*(4-aminophenyl)(6-methylquinolin-2-yl)methanone (**3b**)*. Following the typical procedure (70 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3b** (94% yield, 24.6 mg, Yellow solid, m.p. 201.3-202.1 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.42 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.82-7.88 (m, 4H), 7.68 (d, *J* = 8.8 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 2H), 6.28 (s, 2H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 191.10, 156.27, 154.67, 145.01, 138.15, 136.87, 134.02, 132.91, 129.74, 128.55, 127.08, 123.45, 121.04, 112.94, 21.70. HRMS (EI) m/z: [M] Calcd for $C_{17}H_{14}N_2O$ 262.1106, Found 263.1179 (M+H).

*(4-aminophenyl)(6-methoxyquinolin-2-yl)methanone (**3c**)*. Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3c** 84% yield, 23.3 mg, Yellow solid, m.p. 189.5-190.7 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.48 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 7.91-7.96 (m, 3H), 7.55 (d, *J* = 9.6 Hz, 1H), 7.54 (s, 1H), 6.68 (d, *J* = 8.4 Hz, 2H), 6.31 (s, 2H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.92, 158.87, 154.60, 154.54, 142.34, 136.25, 134.03, 131.56, 129.99, 123.60, 123.34, 121.42, 112.06, 106.13, 56.16. HRMS (EI) m/z: [M] Calcd for $C_{17}H_{14}N_2O_2$ 278.1055, Found 278.1059.

*(4-aminophenyl)(6-fluoroquinolin-2-yl)methanone (**3d**)*. Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3d** (93% yield, 24.7 mg, Yellow solid, m.p. 165.8-167.1 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.53 (d, *J* = 8.4 Hz, 1H), 8.16-8.19 (m, 1H), 7.85-7.92 (m, 4H), 7.76 (dd, *J* = 7.2 Hz, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 2H), 6.32 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.85, 160.93 (d, $J_{F\text{-}C}$ = 245.9 Hz), 156.70 (d, $J_{F\text{-}C}$ = 2.7 Hz), 154.80, 143.60, 137.29 (d, $J_{F\text{-}C}$ = 5.4 Hz), 134.04, 132.93 (d, $J_{F\text{-}C}$ = 9.5 Hz), 129.39 ($J_{F\text{-}C}$ = 10.7 Hz), 123.23, 121.78, 120.88 (d, $J_{F\text{-}C}$ = 25.9 Hz), 112.99, 111.57 (d, $J_{F\text{-}C}$ = 21.9 Hz). HRMS (EI) m/z: [M] Calcd for $C_{16}H_{11}FN_2O$ 266.0855, Found 266.0861.

*(4-aminophenyl)(6-chloroquinolin-2-yl)methanone (**3e**)*. Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3e** (88% yield, 24.8 mg, Yellow solid, m.p. 190.5-191.2 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.53 (d, *J* = 8.4 Hz, 1H), 8.24 (s, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.83-7.87 (m, 3H), 6.63 (d, *J* = 8.0 Hz, 2H), 6.33 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.77, 157.59, 154.87, 144.87, 137.10, 134.02, 132.71, 132.07, 131.29, 129.27, 127.18, 123.11, 121.98, 112.99. HRMS (EI) m/z: [M] Calcd for $C_{16}H_{11}ClN_2O$ 282.0560, Found 282.0563.

*(4-aminophenyl)(7-chloroquinolin-2-yl)methanone (**3f**)*. Following the typical procedure (90 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3f** (86% yield, 24.3 mg, Yellow solid, m.p. 165.4-166.7 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.59 (d, *J* = 8.4 Hz, 1H), 8.16 (s, 1H), 8.13 (d, *J* = 8.8 Hz, 1H), 7.83-7.89 (m, 3H), 7.74 (d, *J* = 8.4 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 2H), 6.34 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.79, 158.27, 154.78, 146.78, 137.88, 135.29, 134.05, 130.45, 128.88, 128.55, 127.10, 123.07, 121.38, 113.01. HRMS (EI) m/z: [M] Calcd for $C_{16}H_{11}ClN_2O$ 282.0560, Found 283.0633 (M+H).

*(4-aminophenyl)(6-bromoquinolin-2-yl)methanone (**3g**)*. Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3g** (90% yield, 29.3 mg, Yellow solid, m.p. 189.4-191.6 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.52 (d, *J* = 8.4 Hz, 1H), 8.39 (s, 1H), 8.04 (d, *J* = 8.8 Hz, 1H), 7.90-7.97 (m, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 6.63 (d, *J* = 8.0 Hz, 2H), 6.33 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.78, 157.65, 154.87, 145.04, 137.00, 134.03, 133.82, 132.11, 130.48, 129.75, 123.10, 121.94, 121.39, 113.00. HRMS (EI) m/z: [M] Calcd for $C_{16}H_{11}BrN_2O$ 326.0055, Found 326.0064.

*methyl 2-(4-aminobenzoyl)quinoline-6-carboxylate (**3h**)*. Following the typical procedure (60 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3h** (65% yield, 19.9 mg, Yellow solid, m.p. 186.4-188.4 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.18 (s, 1H), 8.79 (d, *J* = 8.4 Hz, 1H), 8.31 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J*

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= 8.8 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 6.66 (d, *J* = 8.0 Hz, 2H), 6.38 (s, 2H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.83, 166.26, 159.36, 154.98, 148.25, 139.31, 134.03, 131.25, 130.54, 129.56, 128.84, 127.79, 122.98, 121.80, 113.03, 53.01. HRMS (EI) m/z: [M] Calcd for $C_{18}H_{14}N_2O_3$ 306.1004, Found 306.1013.

*(4-aminophenyl)(quinolin-4-yl)methanone (**3i**).* Following the typical procedure (90 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3i** (95% yield, 23.3 mg, Yellow solid, m.p. 234.0-234.7 °C)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 9.05 (s, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.85 (dd, *J* = 6.8 Hz, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.63 (dd, *J* = 6.8 Hz, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.53 (s, 1H), 6.63 (d, *J* = 8.0 Hz, 2H), 6.50 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 192.63, 155.55, 150.52, 148.30, 146.19, 133.15, 130.34, 129.98, 127.80, 125.80, 125.06, 123.98, 119.41, 113.24. HRMS (EI) m/z: [M] Calcd for $C_{16}H_{12}N_2O$ 248.0950, Found 249.1022 (M+H).

*(4-aminophenyl)(isoquinolin-1-yl)methanone (**3k**).* Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3k** (81% yield, 20.1 mg, Yellow oil)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.56 (d, *J* = 5.2 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 5.2 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.81 (dd, *J* = 7.2 Hz, *J* = 8.0 Hz, 1H), 7.65 (dd, *J* = 7.6 Hz, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 6.60 (d, *J* = 8.4 Hz, 2H), 6.38 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 192.21, 158.82, 155.24, 141.74, 136.37, 133.32, 131.26, 128.58, 127.67, 126.17, 125.62, 123.96, 121.88, 113.11. HRMS (EI) m/z: [M] Calcd for $C_{16}H_{12}N_2O$ 248.0950, Found 249.1022 (M+H).

*(4-aminophenyl)(quinoxalin-2-yl)methanone (**3l**).* Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3l** (85% yield, 21.1 mg, red solid, m.p. 208.8-210.0 °C)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 9.25 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 2H), 7.95-8.01 (m, 2H), 7.89 (d, *J* = 8.4 Hz, 2H), 6.65 (d, *J* = 8.0 Hz, 2H), 6.44 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 189.40, 155.25, 151.42, 145.62, 142.49, 140.16, 134.13, 132.09, 131.51, 130.28, 129.43, 122.86, 113.08. HRMS (EI) m/z: [M] Calcd for $C_{15}H_{11}N_3O$ 249.0902, Found 249.0912.

*(4-aminophenyl)(pyridin-4-yl)methanone (**3m**).* Following the typical procedure (110 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3m** (90% yield, 17.8 mg, Yellow solid)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.73 (d, *J* = 4.0 Hz, 2H), 7.49-7.55 (m, 4H), 6.62 (d, *J* = 8.4 Hz, 2H), 6.38 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 192.26, 155.08, 150.38, 146.74, 133.27, 122.85, 122.73, 113.20. Compound **3m** is known.[20]

*(4-aminophenyl)(benzo[d]thiazol-2-yl)methanone (**3o**).* Following the typical procedure (100 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3o** (86% yield, 21.8 mg, Yellow solid, m.p. 169.5-171.3 °C.)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.41 (d, *J* = 8.4 Hz, 2H), 8.24 (dd, *J* = 9.2 Hz, *J* = 9.6 Hz, 2H), 7.58-7.66 (m, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 6.56 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 180.87, 169.50, 155.73, 153.87, 136.28, 134.38, 127.79, 127.53, 125.40, 123.09, 121.69, 113.11. HRMS (EI) m/z: [M] Calcd for $C_{14}H_{10}N_2OS$ 254.0514, Found 255.0558 (M+H).

*(4-aminophenyl)(6-methoxybenzo[d]thiazol-2-yl)methanone (**3p**).* Following the typical procedure (100 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3p** (90% yield, 25.5 mg, yellow solid, m.p. 182.7-184.6 °C)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.38 (d, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.8 Hz, 1H), 7.78 (s, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 2H), 6.49 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 180.71, 166.90, 159.46, 155.51, 148.38, 138.36, 134.19, 126.20, 121.83, 117.76, 113.26, 104.81, 56.34. HRMS (EI) m/z: [M] Calcd for $C_{15}H_{12}N_2O_2S$ 284.0619, Found 284.0623.

*(4-aminophenyl)(5-bromobenzo[d]thiazol-2-yl)methanone (**3q**).* Following the typical procedure (100 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3q** (80% yield, 26.5 mg,yellow solid, m.p. 186.0-191.3 °C)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.49 (s, 1H), 8.37 (d, *J* = 8.4 Hz, 2H), 8.21 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 2H), 6.60 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 180.47, 171.40, 155.90, 155.00, 135.44, 134.46, 130.50, 127.67, 124.99, 121.41, 120.21, 113.34. HRMS (EI) m/z: [M] Calcd for $C_{14}H_9BrN_2OS$ 331.9619, Found 331.9439.

*(4-amino-3-methylphenyl)(quinolin-2-yl)methanone (**3r**).* Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3r** (84% yield, 22.0 mg, Yellow solid, m.p. 153.5-154.9 °C)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.51 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.82-7.87 (m, 2H), 7.78 (s, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.70 (dd, *J* = 7.2 Hz, *J* = 7.6 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.09 (s, 2H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 191.49, 157.34, 153.05, 146.48, 137.61, 134.03, 132.04, 130.74, 129.97, 128.48, 128.44, 128.28, 123.63, 120.97, 120.31, 112.96, 17.92. HRMS (EI) m/z: [M] Calcd for $C_{17}H_{14}N_2O$ 262.1106, Found 262.1109.

*(4-amino-3-ethylphenyl)(quinolin-2-yl)methanone (**3s**).* Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3s** (82% yield, 21.5 mg, Yellow solid, m.p. 142.1-144.5 °C)**.** ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.55 (d, *J* = 8.4 Hz, 1H), 8.10 (dd, *J* = 9.2 Hz, *J* = 9.2 Hz, 2H), 7.84-7.89 (m, 3H), 7.73 (d, *J* = 7.6 Hz, 2H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.10 (s, 2H), 2.47-2.52 (m, 2H), 1.15 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 191.34, 157.26, 152.43, 146.45, 137.65, 132.08, 131.94, 130.80, 129.93, 128.50, 128.46, 128.35, 125.80, 123.65, 121.02, 113.29, 23.62, 13.35. HRMS (EI) m/z: [M] Calcd for $C_{18}H_{16}N_2O$ 276.1263, Found 262.1261.

(4-amino-3-isopropylphenyl)(quinolin-2-yl)methanone (***3t***). Following the typical procedure (80 °C), after reaction, the mixture

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was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3t** (78% yield, 22.6 mg, red oily liquid). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.54 (d, *J* = 8.4 Hz, 1H), 8.09 (dd, *J* = 8.8 Hz, *J* = 8.8 Hz, 2H), 8.01 (s, 1H), 7.84-7.92 (m, 2H), 7.70-7.72 (m, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.16 (s, 2H), 2.99-3.05 (m, 1H), 1.17 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 191.17, 157.16, 151.84, 146.42, 137.65, 131.76, 130.81, 130.17, 129.91, 129.43, 128.51, 128.47, 128.38, 123.66, 121.08, 113.69, 26.65, 22.63. HRMS (EI) m/z: [M] Calcd for $C_{19}H_{18}N_2O$ 290.1419, Found 290.1423.

(4-amino-3-(tert-butyl)phenyl)(quinolin-2-yl)methanone ***(3u)***. Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3u** (68% yield, 20.7 mg, red oily liquid). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.55 (d, *J* = 8.4 Hz, 1H), 8.15 (s, 1H), 8.09 (dd, *J* = 8.8 Hz, *J* = 8.4 Hz, 2H), 7.84-7.91 (m, 2H), 7.71-7.73 (m, 2H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.04 (s, 2H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 191.10, 157.12, 152.24, 146.40, 137.67, 131.55, 131.14, 130.83, 130.58, 129.90, 128.49, 128.46, 128.39, 123.36, 121.08, 115.82, 34.34, 29.36. HRMS (EI) m/z: [M] Calcd for $C_{20}H_{20}N_2O$ 304.1576, Found 304.1573.

(4-amino-3-methoxyphenyl)(quinolin-2-yl)methanone ***(3v)***. Following the typical procedure (80 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3v** (81% yield, 22.5 mg, Yellow solid, m.p. 177.4-179.1 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.54 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.83-7.91 (m, 2H), 7.68-7.73 (m, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.02 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 191.04, 157.14, 146.45, 145.73, 144.88, 137.66, 130.79, 129.98, 128.61, 128.51, 128.44, 128.37, 123.55, 121.06, 111.98, 111.88, 55.75. HRMS (EI) m/z: [M] Calcd for $C_{17}H_{14}N_2O_2$ 278.1055, Found 278.1059.

(4-amino-3-(trifluoromethoxy)phenyl)(quinolin-2-yl)methanone ***(3w)***. Following the typical procedure (90 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3w** (80% yield, 26.6 mg, Yellow solid, m.p. 188.4-190.1 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.60 (d, *J* = 8.4 Hz, 1H), 8.11-8.15 (m, 3H), 7.95-8.01 (m, 2H), 7.90 (dd, *J* = 7.2 Hz, *J* = 7.6 Hz, 1H), 7.77 (dd, *J* = 7.6 Hz, *J* = 6.8 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.66 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 189.81, 155.86, 147.16, 146.30, 138.00, 133.61, 132.46, 130.99, 129.98, 128.79, 128.76, 128.50, 125.91, 123.08, 121.10 (q, $J_{F\text{-}C}$ = 255.0 Hz), 121.05, 115.35. HRMS (EI) m/z: [M] Calcd for $C_{17}H_{11}F_3N_2O_2$ 332.0773, Found 332.0781.

(4-amino-3-fluorophenyl)(quinolin-2-yl)methanone ***(3x)***. Following the typical procedure (100 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3x** (76% yield, 20.3 mg, Yellow solid, m.p. 146.1-148.2 °C.). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.58 (d, *J* = 7.6 Hz, 1H), 8.09-8.15 (m, 2H), 7.75-7.95 (m, 5H), 6.85 (b, 1H), 6.39 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.35, 156.30, 149.54 ($J_{F\text{-}C}$ = 236.2 Hz), 146.37, 143.10 ($J_{F\text{-}C}$ = 3.0 Hz), 137.91, 130.89, 130.17, 130.08, 128.69, 128.64, 128.48, 123.30 ($J_{F\text{-}C}$ = 5.1 Hz), 121.00, 117.83 ($J_{F\text{-}C}$ = 18.7 Hz), 114.83 ($J_{F\text{-}C}$ = 4.7 Hz). HRMS (EI) m/z: [M] Calcd for $C_{16}H_{11}FN_2O$ 266.0855, Found 266.0861.

(4-amino-3-chlorophenyl)(quinolin-2-yl)methanone ***(3y)***. Following the typical procedure (100 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3y** (80% yield, 22.6 mg, Yellow solid, m.p. 167.8-169.2 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.57 (d, *J* = 8.4 Hz, 1H), 8.08-8.14 (m, 3H), 7.86-7.95 (m, 3H), 7.74 (dd, *J* = 7.2 Hz, *J* = 6.8 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.53 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.15, 156.12, 150.29, 146.34, 137.96, 133.36, 132.20, 130.95, 130.04, 128.72, 128.70, 128.49, 124.40, 121.01, 116.45, 114.44. HRMS (EI) m/z: [M] Calcd for $C_{16}H_{11}ClN_2O$ 282.0560, Found 282.0563.

(4-amino-3-bromophenyl)(quinolin-2-yl)methanone ***(3z)***. Following the typical procedure (100 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3z** (86% yield, 28.1 mg, Yellow solid, m.p. 180.6-182.3 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.57 (d, *J* = 8.4 Hz, 1H), 8.25 (s, 1H), 8.08-8.13 (m, 2H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.87 (dd, *J* = 7.2 Hz, *J* = 8.0 Hz, 1H), 7.74 (dd, *J* = 7.2 Hz, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.49 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 189.96, 156.07, 151.34, 146.34, 137.95, 136.77, 132.70, 130.95, 130.05, 128.72, 128.71, 128.50, 124.90, 121.04, 114.35, 106.39. HRMS (EI) m/z: [M] Calcd for $C_{16}H_{11}BrN_2O$ 326.0055, Found 326.0064.

(4-amino-3-(trifluoromethyl)phenyl)(quinolin-2-yl)methanone ***(3aa)***. Following the typical procedure (110 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3aa** (70% yield, 22.1 mg, Yellow solid, m.p. 166.6-168.2 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.59 (d, *J* = 8.4 Hz, 1H), 8.38 (s, 1H), 8.10-8.14 (m, 3H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.89 (dd, *J* = 7.6 Hz, *J* = 7.6 Hz, 1H), 7.76 (dd, *J* = 7.6 Hz, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.8Hz, 1H), 6.74 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.01, 155.77, 151.02, 146.31, 138.05, 136.23, 131.73 ($J_{F\text{-}C}$ = 5.3 Hz), 131.03, 130.01, 128.84 (b), 128.79, 128.50, 125.06 ($J_{F\text{-}C}$ = 270.4 Hz), 122.73, 121.05 (b), 116.50, 109.84 ($J_{F\text{-}C}$ = 30.1 Hz). HRMS (EI) m/z: [M] Calcd for $C_{17}H_{11}F_3N_2O$ 316.0823, Found 316.0830.

methyl 2-amino-5-(quinoline-2-carbonyl)benzoate ***(3ab)***. Following the typical procedure (110 °C), after reaction, the mixture was diluted with 3-5 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3ab** (70% yield, 21.3 mg, Yellow solid, m.p. 130.2-132.2 °C). ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.77 (s, 1H), 8.57 (d, *J* = 8.4 Hz, 1H), 8.08-8.14 (m, 3H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.87 (dd, *J* = 7.6 Hz, *J* = 7.6 Hz, 1H), 7.74 (dd, *J* = 7.2 Hz, *J* = 7.6 Hz, 1H), 7.59 (s, 2H), 6.92 (d, *J* = 8.8 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.46, 167.79, 156.08, 155.41, 146.38, 137.94, 137.08, 136.48, 130.95, 130.04, 128.73, 128.71, 128.48, 122.93, 121.04, 116.67, 108.37, 52.22. HRMS (EI) m/z: [M] Calcd for $C_{18}H_{14}N_2O_3$ 306.1004, Found 306.1013.

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*(4-aminophenyl)(5,7-dichloro-8-methoxyquinolin-2-yl)methanone (**3ag**).* An oven-dried Schlenk tube containing a stir bar was charged with I_2 (0.2 mmol, 50.8 mg), salicylic acid (0.2 mmol, 28 mg), **1ag** 5,7-dichloro-8-methoxy-2-methylquinoline (1 mmol, 244 mg), the tube was degassed and refilled with O_2 for 3 times. Then 1 mL DMSO and **2a** aniline (3 mmol, 270 uL) were charged under O_2 successively. Then the mixture was stirred at 100 ^oC for 16 h. After reaction, the mixture was diluted with 6 mL DCE, then the volatiles was removed and the residues were passed through a short silica chromatography column to afford analytically pure product **3ag** (78% yield, Yellow solid, m.p. 206.1-207.5 ^oC). ^1H NMR (400 MHz, d_6-DMSO) δ 8.72 (d, *J* = 8.8 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 8.06 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 2H), 6.63 (d, *J* = 8.4 Hz, 2H), 6.37 (s, 2H), 4.09 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 190.11, 157.24, 155.02, 152.00, 141.64, 134.99, 134.16, 129.10, 126.55, 126.47, 125.72, 122.84, 122.64, 112.97, 62.85. HRMS (EI) m/z: [M] Calcd for $C_{17}H_{12}Cl_2N_2O_2$ 346.0276, Found 347.03667 (M+H).

*(E)-(4-(phenyldiazenyl)phenyl)(quinolin-2-yl)methanone (**3ah**).* An oven-dried Schlenk tube containing a stirbar was charged with (4-aminophenyl)(quinolin-2-yl)methanone (3 equiv), and KOH (10 equiv), the tube was degassed and refilled with N_2 for 3 times. Then nitrobenzene (0.5 mmol) and 3 mL DMF were charged under N_2 successively. The reaction mixture was heated at 150 °C for 24 h then cooled to room temperature. The mixture was washed with water and extracted with EtOAc, followed by evaporating the volatiles to obtain the crude product. Purification was done by column chromatography using petroleum ether/ethyl acetate (10:1) to give the pure product **3ah** (71% yield, red solid, m.p. 149.5-151.3 ^oC). ^1H NMR (400 MHz, CD_3Cl) δ 8.35 (d, *J* = 8.0 Hz, 2H), 8.19-8.25 (m, 2H), 8.08 (d, *J* = 8.4 Hz, 2H), 7.93-7.98 (m, 3H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.75 (dd, *J* = 7.2 Hz, *J* = 8.0 Hz, 1H), 7.48-7.56 (m, 4H); ^{13}C NMR (100 MHz, CD_3Cl) δ 156.25, 153.05, 152.79, 148.37, 141.86, 136.94, 132.59, 131.21, 129.88, 129.16, 128.36, 127.53, 127.37, 126.64, 123.41, 123.22, 123.02, 118.98. HRMS (EI) m/z: [M] Calcd for $C_{22}H_{15}N_3O$ 337.1215, Found 337.1225.

*(4-(phenylethynyl)phenyl)(pyridin-4-yl)methanone (**3ai**).* A 10 mL Schlenk flask, charged with $Pd(OAc)_2$ (5 mol%), TFP (15 mol%), a stirring bar and septum, was evacuated and backfilled with N_2 (the cycle was performed three times) and then charged under a positive pressure of N_2 with DMSO (1 mL), (4-aminophenyl)(pyridin-4-yl)methanone (1.3 equiv), AcOH (1.3 equiv), tert-BuONO (1.3 equiv) and phenyl acetylene (0.4 mmol) at room temperature. Then, the Schlenk was transferred to an oil bath and heated at 35 ^oC for 16 hours. The cooled mixture was partitioned between ethyl acetate and saturated NH_4Cl, the organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel to provide the desired product **3ai** (58% yield, Yellow solid, m.p. 158.7-160.2 ^oC). ^1H NMR (400 MHz, d_6-DMSO) δ 8.84 (b, 2H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.76 (d, *J* = 7.6 Hz, 2H), 7.62-7.65 (m, 4H), 7.48 (b, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 194.56, 150.83, 144.21, 135.38, 132.18, 132.10, 130.73, 129.92, 129.36, 127.92, 123.05, 122.08, 93.36, 88.95. HRMS (EI) m/z: [M] Calcd for $C_{20}H_{13}NO$ 283.0997, Found 283.0993.

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Metal-Free Oxidative *para*-Acylation