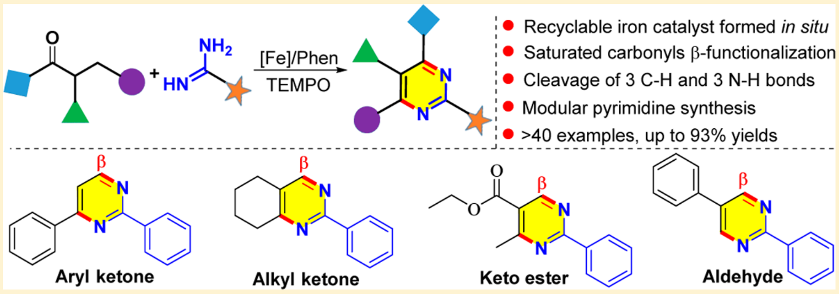
JOC The Journal of Organic Chemistry
Article
pubs.acs.org/joc

Iron Catalysis for Modular Pyrimidine Synthesis through β-Ammoniation/Cyclization of Saturated Carbonyl Compounds with Amidines

Xue-Qiang Chu, Wen-Bin Cao, Xiao-Ping Xu,* and Shun-Jun Ji*

Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science & Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, People's Republic of China

Supporting Information



ABSTRACT: An efficient method for the modular synthesis of various pyrimidine derivatives by means of the reactions of ketones, aldehydes, or esters with amidines in the presence of an in situ prepared recyclable iron(II)-complex was developed. This operationally simple reaction proceeded with broad functional group tolerance in a regioselective manner via a remarkable unactivated β-C−H bond functionalization. Control experiments were performed to gain deep understanding of the mechanism, and the reactions are likely to proceed through a designed TEMPO complexation/enamine addition/transient α-occupation/β-TEMPO elimination/cyclization sequence.

INTRODUCTION

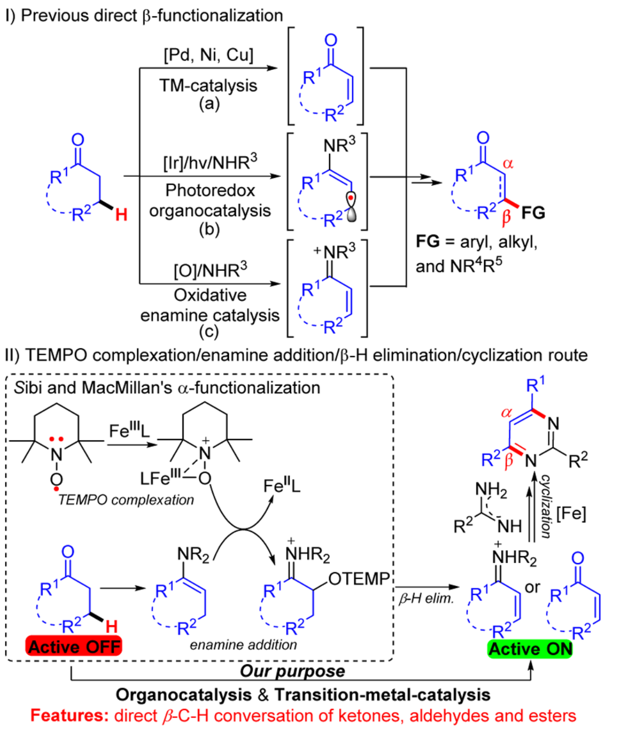
Direct transformation of saturated carbonyl compounds for the rapid assembly of complex molecules from simple starting materials has attracted increasing interest of organic chemists.[1] The site-selectivity challenges involved in the conversion of distant β-C−H bonds of ketones, aldehydes, and esters to new C−X bonds are formidable because the carbonyl moiety is normally amenable to α-position nucleophilic substitution as well as 1,2-functionalizations of the polar C═O bond.[2] Approaches to access β-functionalized carbonyl architecture thus far are mostly restricted to the well-established 1,4-conjugate-addition reactions.[3] Recently, much attention has been directed to transition-metal-catalyzed β-C(sp^3)−H bond cleavage, in which new bonds were selectively constructed by manipulating the reactive sites with elegant directing groups[4] or oxidative dehydrogenative couplings associated with the generation of enone intermediates[5] (Saegusa-type reactions) (Scheme 1, I, route a). Of special note is a photoredox organocatalyzed radical-type enaminyl activation mode reported by MacMillan and co-workers (Scheme 1, I, route b).[6] Another remarkable example involving the oxidation of enamines to iminium ions (oxidative enamine catalysis) also serves as an attractive alternative for the synthesis of β-substituted aldehydes (Scheme 1, I, route c).[7] Although the field of regioselective carbonyl functionalization has grown at an explosive pace, our goal is to develop a robust platform for preparing valuable heterocycle derivatives[8] via a remote β-C−N bond formation strategy beyond that stated above.[5−9]

We envisaged that the intrinsic difficulty of reaction selectivity could be controlled by preinstalling auxiliary amine catalysts in combination with site-occupied reagents. One potential strategy involves the formation of a transient α-occupied iminium ion that showed preference for rapid β-hydride elimination through which to transform an enamine into a desired iminium (or enone) species (Scheme 1, II).[10] Previous reports of Sibi[11a] and MacMillan[11b] suggested the feasibility of this scenario pertaining to the formation of α-oxyaminated aldehydes using Fe(III)−TEMPO (TEMPO = 2,2,6,6-tetramethylpiperidine-*N*-oxyl) adducts,[12] but oxygenation of electron-rich enamine derived from common ketones and further attempts to expand this enamine addition manifold is unknown.[13] In this communication, we report an efficient method for functionalization of unactivated β-C−H bonds of ketones, aldehydes, and esters using a recyclable iron(II)-complex in conjunction with a transient site-controlled TEMPO, which enables the synthesis of a variety of pyrimidines. Control experiments suggest that the reaction

Received: November 18, 2016
Published: December 29, 2016

DOI: 10.1021/acs.joc.6b02767

Scheme 1. β-Functionalization of Saturated Carbonyl Compounds

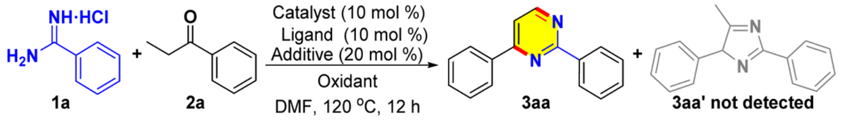


presumably proceeds through a designed TEMPO complexation/enamine addition/transient α-occupation/β-TEMPO elimination/cyclization sequence.

■ RESULTS AND DISCUSSION

Several challenging issues should be dealt with in the proposed process. First is the requirement of suitable catalyst and reagents to realize α-occupation of ketones. Second is utilization of a comparatively inert amine catalyst under oxidative conditions. Third, importantly, is its capacity to undergo subsequent elimination of the stabilized α-substituted iminiums. Finally, an effective system should be compatible with both oxygenation and β-bond-forging cascade. On the basis of the above conjecture and previous reports, our preliminary studies was performed using benzamidine hydrochloride (**1a**) and propiophenone (**2a**) as model substrates in the presence of TEMPO and 2,2,6,6-tetramethylpiperidinium 2,2,2-trifluoroacetate **I** (salt **I**), serving as oxyaminated reagent and organocatalyst, respectively. Fortunately, an inexpensive, earth-abundant, and relatively underrepresented Fe species[14] (10 mol %) in conjunction with 1,10-phenanthroline (Phen) promoted the desired β-aminocyclization reaction to afford the pyrimidine **3aa** in 73% GC yield (Table 1, entry 1). Remarkably, we did not detect any α-functionalized imidazole products, implying that new C−N bond formed exclusively at the terminal position of ketones. Control reactions performed in the absence of TEMPO or Fe catalyst proved to be futile (entries 2−3). Moreover, the ligand Phen was pivotal for providing high yield of **3aa** (entry 4). It is reasonable to assume that reduction of TEMPO by Fe^{2+} to the HTMP (2,2,6,6-tetramethylpiperidine) could save the additional salt **I** used.[12a,c] As expected, the reaction conducted without ammonium salt still could generate **3aa** in 72% GC yield (entry 5), and HTMP was also observed in the catalytic system.[15] However, some accelerating effect of salt **I** on the reaction rate could not be ignored (see Figure S1 in the Supporting Information). After a variety of oxidants (entries 7−9) and iron species were screened (entries 10−14), the optimal reaction conditions were then quickly established by increasing the amount of TEMPO (120 mol %) and changing the iron catalyst to $FeSO_4 \cdot 7H_2O$, which provided **3aa** in 82% GC yield and 79% isolated yield (entry 10). Lower yields and lower selectivities were obtained when other first-row metals such as Co, Ni, and Mn

Table 1. Optimization of Reaction Conditions[a]



	catalyst	additive	ligand	oxidant (equiv)	GC yield (%)
1	$Fe(OAc)_2$	Salt **I**[c]	Phen	TEMPO (1.0)	73
2		Salt **I**[c]	Phen	TEMPO (1.0)	0
3	$Fe(OAc)_2$	Salt **I**[c]	Phen		0
4	$Fe(OAc)_2$	Salt **I**[c]		TEMPO (1.0)	4
5	$Fe(OAc)_2$		Phen	TEMPO (1.0)	72
6	$Fe(OAc)_2$		Phen	TEMPO (1.2)	76
7	$Fe(OAc)_2$		Phen	$K_2S_2O_8$ (1.2)	0
8	$Fe(OAc)_2$		Phen	$PhI(OAc)_2$ (1.2)	0
9	$Fe(OAc)_2$		Phen	TBHP (1.2)	0
10	$FeSO_4 \cdot 7H_2O$		Phen	TEMPO (1.2)	82 (79)[d]
11	$FeCl_2$		Phen	TEMPO (1.2)	trace
12	$FeCl_3$		Phen	TEMPO (1.2)	35
13	$Fe(acac)_3$		Phen	TEMPO (1.2)	62
14	$Fe(NO_3)_3 \cdot 9H_2O$		Phen	TEMPO (1.2)	67
15	Fe complex[e]			TEMPO (1.2)	(81)[d]

[a]Conditions: **1a** (0.3 mmol), **2a** (0.75 mmol), catalyst (0.03 mmol), ligand (0.03 mmol), and oxidant (0.3−0.36 mmol) in DMF (2 mL) at 120 °C under air atmosphere for 12 h. [b]GC yields were determined by GC with an internal standard (biphenyl). [c]Salt **I** = 2,2,6,6-tetramethylpiperidinium 2,2,2-trifluoroacetate. [d]Isolated yield. [e]Fe complex was prepared by mixing $FeSO_4 \cdot 7H_2O$ with Phen in DMF.

DOI: 10.1021/acs.joc.6b02767
J. Org. Chem. 2017, 82, 1145−1154

were used, a reflection of the indispensable role of the Fe species (see Table S1 in the Supporting Information).

As noted in our condition optimization,[15] the reaction proceeded well in DMF, presumably implying that DMF may work as a ligand to iron. Thus, we synthesized a new Fe complex from $FeSO_4 \cdot 7H_2O$ and 1,10-phenanthroline in DMF (Figure 1b). ^1H NMR, IR, ICP, EDS, XPS, and elemental analysis of the obtained red solids pointed out that the structure of the Fe complex was most likely to be $[Fe(Phen)(DMF)_2SO_4]$.[15] This metal complex not only has a good catalytic activity and recyclability (Figure 1c) but also might find further applications in the field of C−H bond functionalization.[14]

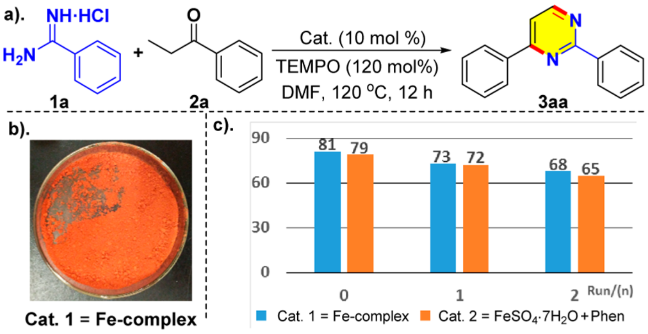


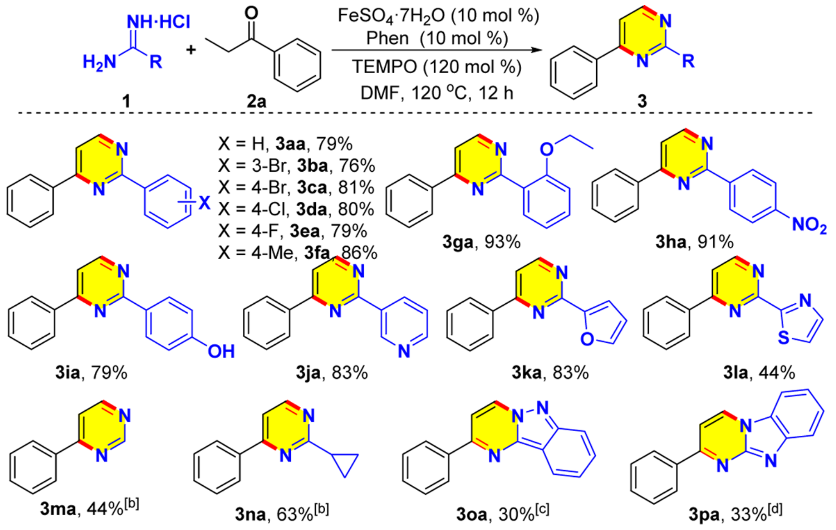
Figure 1. (a) Synthesis of pyrimidine **3aa**. (b) Pre-prepared Fe complex from $FeSO_4 \cdot 7H_2O$ and Phen in DMF. (c) Recyclability of the catalyst.

With the optimal reaction conditions in hand, we explored the scope of amidines using the Fe complex formed in situ, and the results are summarized in Table 2. Generally, benzamidines containing substituents of varying electronic character (electron-donating or electron-withdrawing) and steric demand (*p*-, *m*-, *o*-) on the aryl rings proceeded smoothly to give the corresponding derivatives **3aa−ia** in moderate to good yields. Notably, substituents and functionalities such as halogen (Br, Cl, or F), nitro, and hydroxyl groups were satisfactorily compatible with the present transformation (**3ba−ea** and **3ha−ia**), thereby providing a chance for late-stage structural modifications. Meanwhile, heterocyclic substrates, including pyridine (**1j**), furfuran (**1k**), and thiazole (**1l**) were proven to be appropriate candidates, delivering the products **3ja−la** in 44−83% yields. To our delight, C-alkyl amidines **1m** and **n** were easily transformed into pyrimidines **3ma** and **na** in 44% and 63% yields, respectively. In addition, both 1*H*-indazol-3-amine (**1o**) and 2-benzimidazolylamine (**1p**) could be incorporated into the family of these compounds albeit in relatively low yields, which greatly streamlined access to such condensed nucleus (**3oa−pa**).

The generality of this Fe-catalyzed highly regioselective C−N coupling reaction has been further investigated by using different ketones with amidine **1**. As shown in Table 3, various propiophenones bearing functional groups and substituents, such as halogens, methyl, methoxy, trifluoromethyl and hydroxyl groups as well as biologically interesting benzo[*d*][1,3]dioxole, pyridine, and thiophene heterocycles, were well tolerated under the optimized conditions. It was found that substitutions did not have significant influence on the reaction efficiency, furnishing a variety of 2,4-disubstituted pyrimidines **3ab-cm** in 45%−89% yields. This methodology can be scaled up to 4 mmol scale (**3cc**, 60% yield) without difficulty. Considering that pyrimidine-based heteroaromatics are important pharmaceutical molecules[8a,b] and optoelectronic materials,[8c−f] we were motivated to synthesize more complex *π*-conjugated polycyclic compounds. Thus, ketones **2n−p** derived from parent biphenyl, carbazole, or benzothiophene participated well in the reaction to afford the desired conjugates **3an−ap** in good yields.

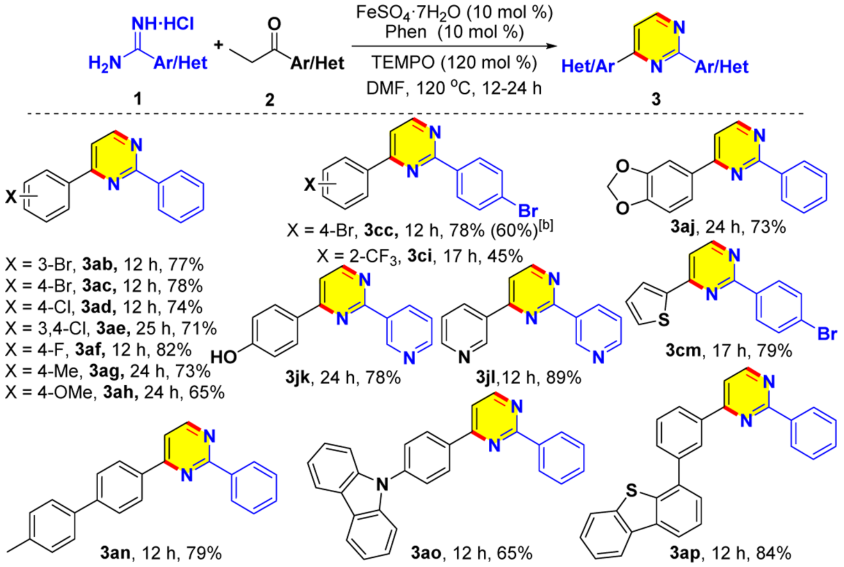
Following the above methods, our attempt to prepare 5-substituted product **5aa** by using isobutyrophenone (**4a**) was unsuccessful, probably due to steric hindrance and the instability of *α*-occupied iminium intermediates (Table 4). In contrast, we were able to accomplish the conversion of *α*-carbonyl ketone to benzoylated product **5ab** in 45% yield, which was extremely difficult to achieve through the functionalization of pyrimidine at its 5-position.[8] Furthermore, *γ*-substituted saturated ketones smoothly underwent the aminocyclization to produce pyrimidine rings **5ac** and **ad** in 53% and 74% yields, respectively. Intriguingly, oxidative

Table 2. Substrate Scope of Amidines[a]



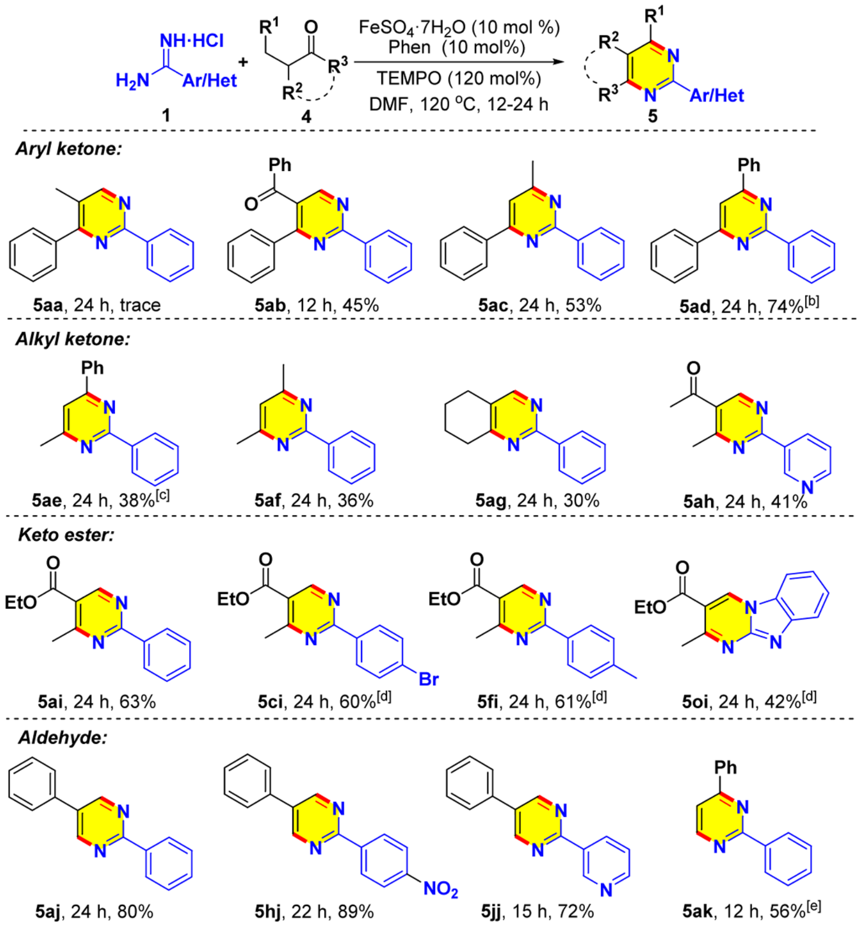
[a]Standard conditions; isolated yields. [b]0.6 mmol scale. [c]17 h. [d]18 h.

Table 3. Substrate Scope of Ketones[a]



[a]Standard conditions; isolated yields. [b]4 mmol scale.

Table 4. Substrate Scope of Carbonyl Compounds[a]



[a]Standard conditions; isolated yields. [b]15 mol % of $FeSO_4·7H_2O$ was used. [c]**5ae** = **5ac**. [d]0.9 mmol of **4i** was used. [e]**5ak** = **3aa**.

dehydrogenative chalcone was isolated as byproduct in this case.[15] Other alkyl ketones such as 4-phenylbutan-2-one (**4e**), pentan-2-one (**4f**), 2-methylcyclohexanone (**4g**), and 3-methylpentane-2,4-dione (**4h**) could also be β-functionalized, although a slightly lower reactivity was observed with aryl ethanones **5ae–ah**. Impressively, acyclic β-keto ester **4**[5d] acted as an effective coupling partner as well (**5ai**, **5ci**, **5fi**, and **5oi**). More importantly, the use of 2-phenylpropanal (**4j**) and 3-phenylpropanal (**4k**)[7] in the reactions provided a concise entry to 3- or 5-substituted pyrimidine fragments in satisfying yields.

Finally, synthetic application was demonstrated to establish modified pyrimidine chromophore **7**, and the photophysical properties were measured by UV−vis absorption (l_{abs} = 272 361 nm), photoluminescence measurements (l_{em} = 476 nm), and cyclic voltammetry (HOMO = −4.85 eV; LUMO = −1.90 eV) (Scheme 2). We tested some pyrimidine derivatives[15] for the antitumor activity against colorectal adenocarcinoma (HT-29), cervical cancer (HeLa), and human pancreatic cancer (PANC-1). Compound **3ah** was found to be very active with EC50 values 0.68−2.12 μM (Table 5), which could be considered as a new potential lead compound for further development because of its biological activity.

Scheme 2. Further Transformation and Its Photophysical Properties

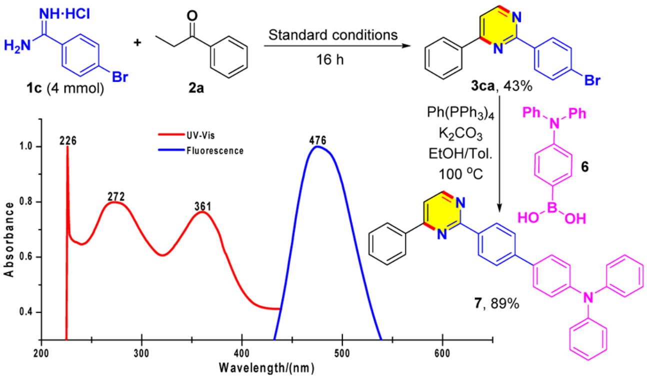


Table 5. Biological Activities of Compounds against Cultured HT-29, HeLa, and PANC-1 Cells[a]

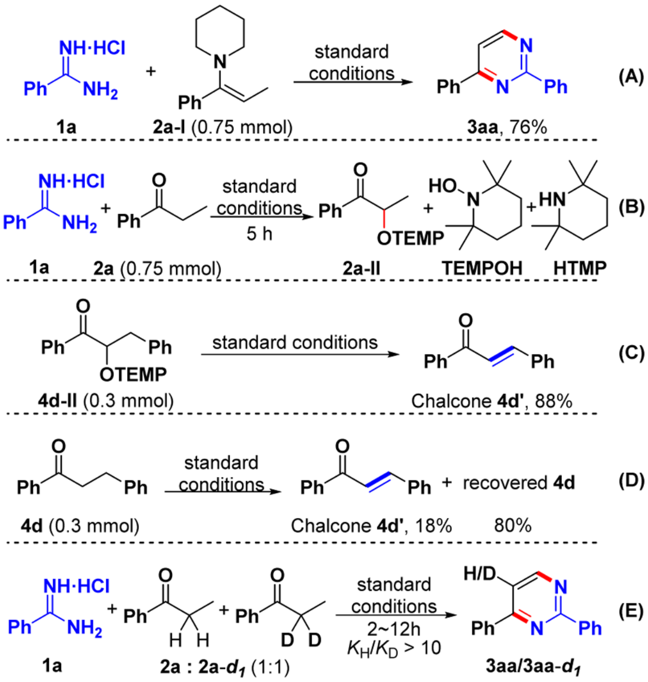
compound	HT-29 EC_{50}, μM	HeLa EC_{50}, μM	PANC-1 EC_{50}, μM
3ah	2.12	0.75	0.68
3pa	23.8	26.4	54.4
3jl	62.35	18.4	19.3
5aj	62.7	53.2	27.4

[a] Selected pyrimidine derivatives were shown.

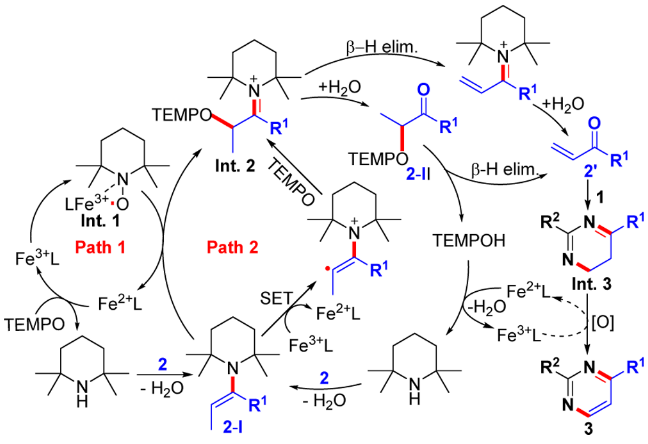
Some control experiments were carried out to gain in-depth insight into the reaction mechanism. First, when **2a** was replaced by pre-prepared enamine **2a-I** under standard conditions, 76% yield of the corresponding product **3aa** was isolated (Scheme 3A). This result revealed that enamine **2a-I** might be formed in situ and most likely contributes to the ammoniation/cyclization. Fortunately, all possible intermediates, including α-oxyaminated ketone **2a-II**, the reduced TEMPOH, and HTMP were detected by LC−MS analysis during the catalytic process (Scheme 3B).[15] Next, α-TEMPO-substituted ketone **4d-II** underwent fast β-TEMPOH elimination to generate dehydrogenative chalcone **4d′** in 88% yield within 2 h (Scheme 3C). By comparison, **4d′** was also observed in the direct oxidation of benzyl acetophenone **4d**; we supposed it went through a process termed transient α-occupied activation (TOA) via active ketone **4d-II** (Scheme 3D). Moreover, intermolecular kinetic isotope effect (KIE) studies indicated that α-C(sp^3)-H bond cleavage of propiophenone was the rate-determining step, and this result was consistent with enamine formation (Scheme 3E).[11,16]

On the basis of these observations and recent reports,[10−12] a plausible mechanism was proposed in Scheme 4. The reaction is initiated with the reduction of TEMPO by $Fe^{2+}L$ to the HTMP,[12a,c] and subsequent condensation with ketone **2** generates enamine **2-I** (Scheme 4, path 1). **Int. 1**, the TEMPO-Fe^{3+} coordinated product,[12] added to enamine **2-I** to form **Int. 2** and $Fe^{2+}L$ (TEMPO complexation/enamine addition stage).[11] **Int. 2** ultimately produced α,β-unsaturated ketone and TEMPOH after iminium hydrolysis and further β-H elimination and vice versa (transient α-occupation/sequential β-TEMPO elimination stage).[10] TEMPOH gives rise to HTMP by $Fe^{2+}L$ in the reaction system. Finally, unsaturated **2′** cyclized with amidine **1** followed by oxidation to furnish pyrimidines (cyclization stage). However, we could not entirely exclude the existence of α-carbonyl radicals (Scheme 4, path 2).[11a,b]

Scheme 3. Control Experiments and Kinetic Isotope Effect Studies



Scheme 4. Proposed Mechanism of Fe-Catalyzed Pyrimidine Synthesis



■ CONCLUSIONS

In summary, we established a novel iron-catalyzed cyclization protocol for accessing modular pyrimidines from readily available saturated carbonyl compounds with amidines. This study led to the development of an unprecedented metal-organocatalytic method for site-selective β-functionalization of unactivated ketones, aldehydes, and esters, involving a TEMPO complexation/enamine addition/transient α-occupation/β-TEMPO elimination/cyclization sequence. Two new C(sp2)-N bonds and a six-membered ring are simultaneously formed in this reaction. Moreover, we accomplished the first β-C−H bond activation system using an in situ formed Fe(II) complex, which is suitable for recycling. We anticipate that the present transformation is capable of offering a new synthetic approach pharmaceutically and biologically important heterocycles.

■ EXPERIMENTAL SECTION

General Procedure for the Synthesis of Pyrimidine Derivatives. Amidine **1** (0.3 mmol), carbonyl compound **2** (0.75 mmol), $FeSO_4\cdot 7H_2O$ (0.03 mmol), 1,10-phenanthroline (Phen, 0.03 mmol), and 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 0.36 mmol) in DMF (2 mL) was stirred at 120 °C for 12−24 h in a tube under air atmosphere. Upon completion of the reaction (indicated by TLC), water (15 mL) was added to the mixture and extracted with ethyl acetate (5 mL × 3). The combined organic extracts were dried with sodium sulfate and concentrated. The pure products were obtained after purification by column chromatography on silica gel with petroleum ether:ethyl acetate (V:V = 100:1−20:1) as the eluent.

General Procedure for the Large Scale Synthesis of Pyrimidine Derivatives. Amidine **1c** (4 mmol), carbonyl compound **2** (10 mmol), $FeSO_4\cdot 7H_2O$ (0.4 mmol), Phen (0.4 mmol), and TEMPO (4.8 mmol) in DMF (15 mL) were stirred at 120 °C for 16 h in a tube under air atmosphere. Upon completion of the reaction (indicated by TLC), water (30 mL) was added to the mixture and extracted with ethyl acetate (15 mL × 3). The combined organic extracts were dried with sodium sulfate and concentrated. The pure products were obtained after purification by column chromatography on silica gel with petroleum ether:ethyl acetate (V:V = 100:1−20:1) as the eluent (white solid, 43% yield).

General Procedure for the Synthesis of Compound 7. Pyrimidine **3ca** (1.55 mmol), 4-(diphenylamino)phenylboronic acid **6** (2.33 mmol), $Pd(PPh_3)_4$ (0.155 mmol), and K_2CO_3 (3.88 mmol) were stirred at 100 °C for 17 h under an Ar atmosphere in ethanol/toluene (40 mL, V:V = 1:4). Upon completion of the reaction (indicated by TLC), the solvents were removed under vacuum. The pure products were obtained after purification by column chromatography on silica gel with petroleum ether:ethyl acetate (V:V = 100:1) as the eluent (yellow solid, 89% yield).

Analytical Data of Products. *2,4-Diphenylpyrimidine (**3aa**) and (**5aj**).* Yield = 79% (0.0553 g) (**3aa**), 56% (0.0388 g) (**5aj**) . White solid. Mp 56.3−57.8 °C. IR (KBr) ν = 2972, 2922, 1541, 1422, 1378, 1027, 745, and 687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, J = 5.3 Hz, 1H), 8.63−8.54 (m, 2H), 8.27−8.18 (m, 2H), 7.58 (d, J = 5.3 Hz, 1H), 7.56−7.48 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7, 164.0, 158.0, 138.0, 137.1, 131.1, 130.8, 129.1, 128.7, 128.4, 127.3, 114.6 ppm. HRMS m/z: calcd for $C_{16}H_{13}N_2$ $[M + H]^+$ 233.1073, found: 233.1077.

*2-(3-Bromophenyl)-4-phenylpyrimidine (**3ba**).* Yield = 76% (0.0710 g). Yellow oil. IR (KBr) ν = 3064, 2925, 1575, 1435, 1256, 1067, 846, 789, and 684 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.83 (d, J = 5.3 Hz, 1H), 8.74 (t, J = 1.8 Hz, 1H), 8.54−8.49 (m, 1H), 8.25−8.18 (m, 2H), 7.64−7.60 (m, 2H), 7.57−7.53 (m, 3H), 7.38 (t, J = 7.9 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.2, 163.3, 158.0, 140.0, 136.8, 133.7, 131.4, 131.3, 130.2, 129.1, 127.4, 127.0, 123.0, 115.1 ppm. HRMS m/z: calcd for $C_{16}H_{12}BrN_2$ $[M + H]^+$ 311.0178, found: 311.0189.

*2-(4-Bromophenyl)-4-phenylpyrimidine (**3ca**).* Yield = 81% (0.0759 g). White solid. Mp 85.9−87.7 °C. IR (KBr) ν = 2987, 2901, 1578, 1543, 1377, 1065, 1006, 837, 765, and 695 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, J = 5.3 Hz, 1H), 8.51−8.42 (m, 2H), 8.25−8.17 (m, 2H), 7.68−7.59 (m, 3H), 7.57−7.51 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 163.9, 158.0, 136.9, 136.9, 131.9, 131.2, 130.0, 129.1, 127.3, 125.6, 114.9 ppm. HRMS m/z: calcd for $C_{16}H_{12}BrN_2$ $[M + H]^+$ 311.0178, found: 311.0188.

*2-(4-Chlorophenyl)-4-phenylpyrimidine (**3da**).* Yield = 80% (0.0637 g). White solid. Mp 98.0−101.0 °C. IR (KBr) ν = 2967, 2922, 1557, 1400, 1087, 833, 765, and 687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.84−8.78 (m, 1H), 8.56−8.48 (m, 2H), 8.24−8.17 (m, 2H), 7.62−7.58 (m, 1H), 7.56−7.51 (m, 3H), 7.50−7.45 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 163.8, 158.0, 137.1, 136.9, 136.5, 131.2, 129.8, 129.1, 128.9, 127.3, 114.8 ppm. HRMS m/z: calcd for $C_{16}H_{12}ClN_2$ $[M + H]^+$ 267.0684, found: 267.0694.

*2-(4-Fluorophenyl)-4-phenylpyrimidine (**3ea**).* Yield = 82% (0.0616 g). White solid. Mp 61.2−61.3 °C. IR (KBr) ν = 2975, 2854, 1565, 1508, 1404, 1219, 1150, 828, 763, and 686 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (d, J = 5.2 Hz, 1H), 8.64−8.54 (m, 2H), 8.27−8.17 (m, 2H), 7.59 (d, J = 5.3 Hz, 1H), 7.56−7.50 (m, 3H), 7.23−7.14 (m, 2H) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = −110.5 ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.0 (d, J_{C-F} = 228.8 Hz), 163.8 (d, J_{C-F} = 43.5 Hz), 158.0, 137.0, 134.2 (d, J_{C-F} = 2.9 Hz), 131.2, 130.5 (d, J_{C-F} = 8.7 Hz), 129.1, 127.3, 115.7, 115.5, 114.6 ppm. HRMS m/z: calcd for $C_{16}H_{12}FN_2$ $[M + H]^+$ 251.0979, found: 251.0973.

*4-Phenyl-2-p-tolylpyrimidine (**3fa**).* Yield = 86% (0.0632 g). White solid. Mp 78.3−79.0 °C. IR (KBr) ν = 2919, 2854, 1581, 1424, 1381, 1276, 1175, 830, 764, and 688 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (d, J = 5.2 Hz, 1H), 8.50−8.45 (m, 2H), 8.26−8.19 (m, 2H), 7.57 (d, J = 5.3 Hz, 1H), 7.53 (dd, J = 5.1, 2.0 Hz, 3H), 7.32 (d, J = 8.0 Hz, 2H), 2.44 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8, 163.9, 157.9, 141.1, 137.2, 135.3, 131.0, 129.4, 129.1, 128.4, 127.3, 114.4, 21.7 ppm. HRMS m/z: calcd for $C_{17}H_{15}N_2$ $[M + H]^+$ 247.1230, found: 247.1220.

*2-(2-Ethoxyphenyl)-4-phenylpyrimidine (**3ga**).* Yield = 93% (0.0772 g). White solid. Mp 40.2−41.6 °C. IR (KBr) ν = 2983, 2926, 1582, 1422, 1242, 1107, 1041, 756, and 691 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.94 (d, J = 5.3 Hz, 1H), 8.31−8.24 (m, 2H), 7.99 (d, J = 5.3 Hz, 1H), 7.69 (dd, J = 7.6, 1.8 Hz, 1H), 7.60−7.54 (m, 3H), 7.49−7.42 (m, 1H), 7.18 (d, J = 8.2 Hz, 1H), 7.11−7.04 (m, 1H), 4.16−4.06 (m, 2H), 1.27 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 162.5, 158.1, 156.9, 136.4, 131.2, 131.1, 130.8, 129.0, 128.9, 127.1, 120.3, 114.4, 113.7, 64.0, 14.7 ppm. HRMS m/z: calcd for $C_{18}H_{17}N_2O$ $[M + H]^+$ 277.1335, found: 277.1344.

*2-(4-Nitrophenyl)-4-phenylpyrimidine (**3ha**).* Yield = 91% (0.0756 g). White solid. Mp 181.7−182.5 °C. IR (KBr) ν = 2987, 2901, 1564, 1394, 1250, 1066, 741, and 690 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.06 (d, J = 5.3 Hz, 1H), 8.80−8.73 (m, 2H), 8.42 (d, J = 2.0 Hz, 1H), 8.41−8.35 (m, 3H), 8.15 (d, J = 5.3 Hz, 1H), 7.66−7.59 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.4, 162.6, 158.2, 149.4, 143.7, 136.5, 131.5, 129.3, 129.2, 127.4, 123.8, 115.7 ppm. HRMS m/z: calcd for $C_{16}H_{12}N_3O_2$ $[M + H]^+$ 278.0924, found: 278.0927.

*4-(4-Phenylpyrimidin-2-yl)phenol (**3ia**).* Yield = 89% (0.0663 g). White solid. Mp 201.9−202.3 °C. IR (KBr) ν = 2987, 2901, 1566, 1417, 1274, 1236, 1167, 1066, 766, and 690 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.87 (d, J = 5.3 Hz, 1H), 8.43−8.37 (m, 2H), 8.36−8.29 (m, 2H), 7.89 (d, J = 5.3 Hz, 1H), 7.64−7.55 (m, 3H), 6.98−6.90 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.5, 162.6, 160.2, 158.4, 136.4, 131.1, 129.6, 129.0, 128.3, 127.0, 115.4, 113.9 ppm. HRMS m/z: calcd for $C_{16}H_{13}N_2O$ $[M + H]^+$ 249.1022, found: 249.1019.

*4-Phenyl-2-(pyridin-3-yl)pyrimidine (**3ja**).* Yield = 83% (0.0583 g). White solid. Mp 80.8−81.0 °C. IR (KBr) ν = 2987, 2901, 1581, 1417, 1370, 1066, 824, 758, and 686 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.83−9.73 (m, 1H), 8.86 (d, J = 5.3 Hz, 1H), 8.84−8.80 (m, 1H), 8.74 (dd, J = 5.0, 1.7 Hz, 1H), 8.28−8.18 (m, 2H), 7.67 (d, J = 5.3 Hz, 1H), 7.61–7.52 (m, 3H), 7.48–7.42 (m, 1H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 164.2, 163.0, 158.1, 151.5, 150.2, 136.7, 135.7, 133.5, 131.4, 129.2, 127.4, 123.5, 115.3 ppm. HRMS m/z: calcd for $C_{15}H_{12}N_3$ [M + H]$^+$ 234.1026, found: 234.1037.

*2-(Furan-3-yl)-4-phenylpyrimidine (**3ka**).* Yield = 83% (0.0552 g). Yellow oil. IR (KBr) ν = 3061, 2928, 1683, 1587, 1489, 1450, 1224, 1006, 921, 765, and 695 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.88 (d, J = 5.3 Hz, 1H), 8.34–8.24 (m, 2H), 7.98–7.96 (m, 1H), 7.94 (d, J = 5.3 Hz, 1H), 7.63–7.55 (m, 3H), 7.45–7.40 (m, 1H), 6.76–6.71 (m, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9, 158.5, 157.1, 151.9, 145.8, 135.9, 131.3, 129.0, 127.1, 114.6, 113.6, 112.5 ppm. HRMS m/z: calcd for $C_{14}H_{11}N_2O$ [M + H]$^+$ 223.0866, found: 223.0869.

*2-(4-Phenylpyrimidin-2-yl)thiazole (**3la**).* Yield = 44% (0.0315 g). White solid. Mp 74.3–76.8 °C. IR (KBr) ν = 3074, 2968, 1673, 1570, 1429, 1264, 1068, 775, and 692 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.00 (d, J = 5.4 Hz, 1H), 8.35–8.29 (m, 2H), 8.15 (d, J = 5.3 Hz, 1H), 8.13 (d, J = 3.1 Hz, 1H), 8.03 (d, J = 3.1 Hz, 1H), 7.65–7.60 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.5, 163.5, 159.0, 158.9, 145.1, 135.4, 131.6, 129.1, 127.2, 124.5, 116.7 ppm. HRMS m/z: calcd for $C_{13}H_{10}N_3S$ [M + H]$^+$ 240.0590, found: 240.0595.

*4-Phenylpyrimidine (**3ma**).* Yield = 44% (0.0414 g). Yellow oil. IR (KBr) ν = 2924, 2835, 1671, 1576, 1387, 1179, 1074, 744, and 691 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.25 (d, J = 1.4 Hz, 1H), 8.87 (d, J = 5.4 Hz, 1H), 8.25–8.19 (m, 2H), 8.12–8.09 (m, 1H), 7.60–7.54 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.6, 158.8, 158.1, 136.0, 131.3, 129.1, 127.0, 117.2 ppm. HRMS m/z: calcd for $C_{10}H_9N_2$ [M + H]$^+$ 157.0760, found: 157.0768.

*2-Cyclopropyl-4-phenylpyrimidine (**3na**).* Yield = 63% (0.0735 g). Yellow oil. IR (KBr) ν = 3008, 1568, 1546, 1436, 1026, 917, 763, and 690 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.68 (d, J = 5.3 Hz, 1H), 8.21–8.14 (m, 2H), 7.81 (d, J = 5.3 Hz, 1H), 7.58–7.52 (m, 3H), 2.26 (tt, J = 7.8, 5.4 Hz, 1H), 1.11–1.05 (m, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 171.1, 162.4, 158.0, 136.3, 131.0, 128.9, 126.9, 113.8, 18.0, 10.4 ppm. HRMS m/z: calcd for $C_{13}H_{13}N_2$ [M + H]$^+$ 197.1073, found: 197.1078.

*2-Phenylpyrimido[1,2-b]indazole (**3oa**).* Yield = 30% (0.0220 g). White solid. Mp 104.9–105.1 °C. IR (KBr) ν = 3049, 2921, 2851, 1634, 1534, 1413, 1228, 811, 722, and 684 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.49 (d, J = 7.4 Hz, 1H), 8.43–8.36 (m, 2H), 8.35–8.30 (m, 1H), 8.13 (d, J = 7.4 Hz, 1H), 7.82 (d, J = 8.6 Hz, 1H), 7.69–7.55 (m, 4H), 7.36–7.30 (m, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.1, 151.0, 142.7, 136.3, 135.2, 130.5, 129.8, 129.1, 127.1, 120.7, 120.6, 116.1, 112.9, 109.4 ppm. HRMS m/z: calcd for $C_{16}H_{12}N_3$ [M + H]$^+$ 246.1026, found: 246.1037.

*2-Phenylbenzo[4,5]imidazo[1,2-a]pyrimidine (**3pa**).* Yield = 33% (0.0244 g). White solid. Mp 257.5–257.2 °C. IR (KBr) ν = 2960, 2922, 2853, 1604, 1522, 1455, 1419, 1257, 1026, and 755 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.61 (d, J = 7.2 Hz, 1H), 8.42–8.29 (m, 3H), 7.89–7.80 (m, 2H), 7.66–7.59 (m, 3H), 7.55 (t, J = 7.7 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.0, 150.3, 144.3, 136.5, 136.1, 131.4, 129.1, 127.6, 127.1, 126.0, 121.3, 119.0, 112.5, 103.9 ppm. HRMS m/z: calcd for $C_{16}H_{12}N_3$ [M + H]$^+$ 246.1026, found: 246.1034.

*4-(3-Bromophenyl)-2-phenylpyrimidine (**3ab**).* Yield = 77% (0.0716 g). White solid. Mp 69.1–70.7 °C. IR (KBr) ν = 2987, 2901, 1587, 1410, 1263, 1067, 749, and 696 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.00 (d, J = 5.3 Hz, 1H), 8.55–8.49 (m, 3H), 8.36 (d, J = 7.8 Hz, 1H), 8.08 (d, J = 5.3 Hz, 1H), 7.80 (dd, J = 7.9, 2.0 Hz, 1H), 7.61–7.54 (m, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.4, 161.4, 158.9, 138.6, 137.1, 133.9, 131.2, 131.0, 129.6, 128.7, 127.8, 126.2, 122.6, 115.4 ppm. HRMS m/z: calcd for $C_{16}H_{12}BrN_2$ [M + H]$^+$ 311.0178, found: 311.0189.

*4-(4-Bromophenyl)-2-phenylpyrimidine (**3ac**).* Yield = 78% (0.0728 g). White solid. Mp 99.8–100.1 °C. IR (KBr) ν = 3059, 2922, 1586, 1539, 1425, 1371, 1068, 1002, 814, 749, and 689 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.99 (d, J = 5.3 Hz, 1H), 8.56–8.49 (m, 2H), 8.36–8.28 (m, 2H), 8.04 (d, J = 5.4 Hz, 1H), 7.85–7.77 (m, 2H), 7.62–7.54 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.4, 161.8, 158.9, 137.2, 135.4, 132.1, 131.0, 129.1, 128.7, 127.8, 125.1, 115.0 ppm. HRMS m/z: calcd for $C_{16}H_{12}BrN_2$ [M + H]$^+$ 311.0178, found: 311.0187.

*4-(4-Chlorophenyl)-2-phenylpyrimidine (**3ad**).* Yield = 74% (0.0588 g). White solid. Mp 83.0–83.4 °C. IR (KBr) ν = 2987, 2971, 1561, 1541, 1455, 1377, 1086, 816, 750, and 670 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.99 (d, J = 5.3 Hz, 1H), 8.57–8.50 (m, 2H), 8.43–8.35 (m, 2H), 8.04 (d, J = 5.3 Hz, 1H), 7.70–7.64 (m, 2H), 7.61–7.54 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.3, 161.7, 158.9, 137.2, 136.1, 135.0, 131.0, 129.1, 128.9, 128.7, 127.8, 115.1 ppm. HRMS m/z: calcd for $C_{16}H_{12}ClN_2$ [M + H]$^+$ 267.0684, found: 267.0693.

*4-(3,4-Dichlorophenyl)-2-phenylpyrimidine (**3ae**).* Yield = 71% (0.0638 g). White solid. Mp 90.1–91.7 °C. IR (KBr) ν = 2987, 2901, 1561, 1425, 1396, 1260, 1066, 825, 751, and 686 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.02 (d, J = 5.3 Hz, 1H), 8.62–8.48 (m, 3H), 8.38–8.32 (m, 1H), 8.12 (d, J = 5.3 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.60–7.54 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.4, 160.6, 159.1, 137.0, 136.8, 134.0, 132.1, 131.3, 131.1, 128.8, 128.8, 127.9, 127.2, 115.4 ppm. HRMS m/z: calcd for $C_{16}H_{11}Cl_2N_2$ [M + H]$^+$ 301.0294, found: 301.0292.

*4-(4-Fluorophenyl)-2-phenylpyrimidine (**3af**).* Yield = 82% (0.0613 g). White solid. Mp 46.7–47.0 °C. IR (KBr) ν = 2987, 2970, 2922, 1565, 1505, 1431, 1408, 1227, 1157, 827, 756, and 689 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.97 (d, J = 5.3 Hz, 1H), 8.58–8.50 (m, 2H), 8.48–8.40 (m, 2H), 8.02 (d, J = 5.3 Hz, 1H), 7.61–7.54 (m, 3H), 7.44 (t, J = 8.7 Hz, 2H) ppm. ^{19}F NMR (376 MHz, DMSO-d_6): δ = δ −109.6 ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.1 (d, J_{C-F} = 247.5 Hz), 162.6 (d, J_{C-F} = 142.8 Hz), 158.7, 137.2, 132.7 (d, J_{C-F} = 3.0 Hz), 130.9, 129.6 (d, J_{C-F} = 8.7 Hz), 128.7, 127.8, 116.1, 115.9, 114.9 ppm. HRMS m/z: calcd for $C_{16}H_{12}FN_2$ [M + H]$^+$ 251.0979, found: 251.0981.

*2-Phenyl-4-p-tolylpyrimidine (**3ag**).* Yield = 73% (0.0537 g). White solid. Mp 98.3–99.3 °C. IR (KBr) ν = 2987, 2901, 1562, 1544, 1426, 1075, 813, 757, and 693 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.93 (d, J = 5.3 Hz, 1H), 8.57–8.49 (m, 2H), 8.30–8 0.23 (m, 2H), 7.98 (d, J = 5.3 Hz, 1H), 7.61–7.53 (m, 3H), 7.41 (d, J = 8.0 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.2, 162.8, 158.5, 141.3, 137.4, 133.4, 130.8, 129.7, 128.7, 127.8, 127.0, 114.7, 21.0 ppm. HRMS m/z: calcd for $C_{17}H_{15}N_2$ [M + H]$^+$ 247.1230, found: 247.1243.

*4-(4-Methoxyphenyl)-2-phenylpyrimidine (**3ah**).* Yield = 65% (0.0509 g). White solid. Mp 167.4–169.9 °C. IR (KBr) ν = 2987, 2970, 2901, 1584, 1560, 1412, 1380, 1250, 1179, 1025, 827, 757, and 692 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.89 (d, J = 5.3 Hz, 1H), 8.58–8.48 (m, 2H), 8.40–8.29 (m, 2H), 7.94 (d, J = 5.4 Hz, 1H), 7.63–7.52 (m, 3H), 7.19–7.10 (m, 2H), 3.87 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.1, 162.5, 161.9, 158.3, 137.5, 130.8, 128.8, 128.7, 128.5, 127.7, 114.4, 114.2, 55.4 ppm. HRMS m/z: calcd for $C_{17}H_{15}N_2O$ [M + H]$^+$ 263.1179, found: 263.1185.

*2,4-Bis(4-bromophenyl)pyrimidine (**3cc**).* Yield = 78% (0.0914 g). White solid. Mp 160.4–161.8 °C. IR (KBr) ν = 2987, 2922, 1577, 1538, 1434, 1069, 1007, 815, and 786 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.97 (d, J = 5.3 Hz, 1H), 8.49–8.40 (m, 2H), 8.33–8.25 (m, 2H), 8.05 (d, J = 5.3 Hz, 1H), 7.83–7.73 (m, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.5, 161.9, 159.0, 136.4, 135.2, 132.1, 131.8, 129.8, 129.2, 125.2, 124.9, 115.3 ppm. HRMS m/z: calcd for $C_{16}H_{11}Br_2N_2$ [M + H]$^+$ 388.9283, found: 388.9280.

*2-(4-Bromophenyl)-4-(2-(trifluoromethyl)phenyl)pyrimidine (**3ci**).* Yield = 45% (0.0507 g). White solid. Mp 72.9–73.4 °C. IR (KBr) ν = 2987, 2901, 1543, 1373, 1315, 1165, 1090, 1036, 837, and 769 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.05 (d, J = 5.1 Hz, 1H), 8.41–8.30 (m, 2H), 8.01–7.93 (m, 1H), 7.87 (t, J = 7.2 Hz, 1H), 7.83–7.71 (m, 4H), 7.68 (d, J = 5.1 Hz, 1H) ppm. ^{19}F NMR (376 MHz, DMSO-d_6): δ = δ −55.2 ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.2, 161.9, 158.4, 137.1 (q, J_{C-F} = 3.6, 1.5 Hz), 136.1, 132.7, 131.9, 131.5, 130.1, 129.7, 126.9 (q, J_{C-F} = 236.6, 5.16 Hz), 125.3, 125.0, 122.6, 119.3 ppm. HRMS m/z: calcd for $C_{17}H_{11}BrF_3N_2$ [M + H]$^+$ 379.0052, found: 379.0067.

*4-(Benzo[d][1,3]dioxol-5-yl)-2-phenylpyrimidine (**3aj**).* Yield = 73% (0.0608 g). White solid. Mp 116.2–118.4 °C. IR (KBr) ν =

2970, 2920, 1560, 1442, 1251, 1033, 799, 755, and 698 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.89 (d, J = 5.3 Hz, 1H), 8.56−8.48 (m, 2H), 7.99−7.95 (m, 1H), 7.95−7.89 (m, 2H), 7.59−7.53 (m, 3H), 7.12 (d, J = 8.2 Hz, 1H), 6.16 (s, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.1, 162.3, 158.3, 150.0, 148.2, 137.4, 130.8, 130.3, 128.7, 127.8, 122.1, 114.4, 108.7, 106.9, 101.8 ppm. HRMS m/z: calcd for $C_{17}H_{13}N_2O_2$ [M + H]$^+$ 277.0972, found: 277.0982.

4-(2-(Pyridin-3-yl)pyrimidin-4-yl)phenol (**3jk**). Yield = 78% (0.0582 g). White solid. Mp 254.1−256.9. IR (KBr) ν = 3095, 3021, 1588, 1508, 1406, 1281, 1035, 826, 781, and 698 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.16 (s, 1H), 9.63 (s, 1H), 8.89 (d, J = 5.4 Hz, 1H), 8.84−8.69 (m, 2H), 8.26 (d, J = 8.3 Hz, 2H), 7.94 (d, J = 5.4 Hz, 1H), 7.59 (dd, J = 8.0, 4.8 Hz, 1H), 6.96 (d, J = 8.3 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.0, 161.6, 160.7, 158.2, 151.4, 149.0, 135.1, 133.0, 129.0, 126.6, 123.8, 115.9, 114.4 ppm. HRMS m/z: calcd for $C_{15}H_{12}N_3O$ [M + H]$^+$ 250.0975, found: 250.0985.

2,4-Di(pyridin-3-yl)pyrimidine (**3jl**). Yield = 89% (0.0626 g). White solid. Mp 133.8−134.2 °C. IR (KBr) ν = 2987, 2901, 1583, 1408, 1025, 783, and 698 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.66 (d, J = 2.2 Hz, 1H), 9.53 (d, J = 2.3 Hz, 1H), 9.07 (d, J = 5.3 Hz, 1H), 8.87−8.70 (m, 4H), 8.20 (d, J = 5.3 Hz, 1H), 7.67−7.57 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.0, 161.4, 159.1, 152.0, 151.6, 149.1, 148.5, 135.3, 134.8, 132.6, 131.6, 124.1, 123.9, 116.1 ppm. HRMS m/z: calcd for $C_{14}H_{11}N_4$ [M + H]$^+$ 235.0978, found: 235.0981.

2-(4-Bromophenyl)-4-(thiophen-2-yl)pyrimidine (**3cm**). Yield = 79% (0.0751 g). White solid. Mp 104.9−105.7 °C. IR (KBr) ν = 2968, 2854, 1555, 1396, 1064, 822, 785, and 700 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.89 (d, J = 5.3 Hz, 1H), 8.42−8.33 (m, 2H), 8.15 (dd, J = 3.8, 1.2 Hz, 1H), 7.94 (d, J = 5.3 Hz, 1H), 7.89 (dd, J = 5.0, 1.1 Hz, 1H), 7.81−7.75 (m, 2H), 7.30 (dd, J = 5.0, 3.7 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.4, 158.7, 158.4, 141.8, 136.1, 131.8, 131.5, 129.6, 129.2, 129.0, 124.9, 113.7 ppm. HRMS m/z: calcd for $C_{14}H_{10}BrN_2S$ [M + H]$^+$ 316.9743, found: 316.9746.

4-(4′-Methylbiphenyl-4-yl)-2-phenylpyrimidine (**3an**). Yield = 79% (0.0761 g). White solid. Mp 162.1−163.4 °C. IR (KBr) ν = 2987, 2901, 1557, 1415, 1066, 806, 759, and 692 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.97 (d, J = 5.3 Hz, 1H), 8.58−8.63 (m, 2H), 8.48−8.40 (m, 2H), 8.06 (d, J = 5.3 Hz, 1H), 7.92−7.84 (m, 2H), 7.72−7.65 (m, 2H), 7.61−7.55 (m, 3H), 7.33 (d, J = 7.8 Hz, 2H), 2.37 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.3, 162.5, 158.6, 142.7, 137.6, 137.4, 136.3, 134.8, 130.9, 129.7, 128.7, 127.8, 127.7, 127.0, 126.6, 115.0, 20.7 ppm. HRMS m/z: calcd for $C_{23}H_{19}N_2$ [M + H]$^+$ 323.1543, found: 323.1547.

9-(4-(2-Phenylpyrimidin-4-yl)phenyl)-9H-carbazole (**3ao**). Yield = 65% (0.0771 g). White solid. Mp 187.3−189.0 °C. IR (KBr) ν = 3063, 2923, 2853, 1561, 1449, 1228, 829, 746, and 696 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.05 (d, J = 5.3 Hz, 1H), 8.67 (d, J = 8.5 Hz, 2H), 8.61−8.56 (m, 2H), 8.29 (d, J = 7.8 Hz, 2H), 8.15 (d, J = 5.3 Hz, 1H), 7.92−7.85 (m, 2H), 7.62−7.57 (m, 3H), 7.54 (d, J = 8.2 Hz, 2H), 7.51−7.45 (m, 2H), 7.37−7.31 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.9, 163.1, 158.2, 140.6, 140.4, 137.9, 135.8, 131.0, 128.9, 128.7, 128.5, 127.3, 126.3, 123.8, 120.6, 120.5, 114.6, 109.9 ppm. HRMS m/z: calcd for $C_{28}H_{20}N_3$ [M + H]$^+$ 398.1652, found: 398.1645.

4-(3-(Dibenzo[b,d]thiophen-4-yl)phenyl)-2-phenylpyrimidine (**3ap**). Yield = 84% (0.1041 g). White solid. Mp 53.2−55.1 °C. IR (KBr) ν = 2987, 2901, 1560, 1420, 1379, 1255, 1049, 744, and 691 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.19 (d, J = 5.3 Hz, 1H), 7.94 (s, 1H), 7.83−7.74 (m, 2H), 7.69−7.57 (m, 3H), 7.28 (d, J = 5.3 Hz, 1H), 7.26−7.19 (m, 1H), 7.17−7.10 (m, 1H), 6.98 (t, J = 7.8 Hz, 1H), 6.92−6.85 (m, 2H), 6.78−6.72 (m, 5H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.4, 162.6, 158.7, 140.5, 138.4, 137.4, 137.2, 137.0, 135.9, 135.6, 135.2, 130.8, 130.6, 129.8, 128.6, 127.8, 127.3, 127.1, 126.9, 126.5, 125.7, 124.8, 122.8, 122.2, 121.4, 115.3 ppm. HRMS m/z: calcd for $C_{28}H_{19}N_2S$ [M + H]$^+$ 415.1263, found: 415.1275.

(2,4-Diphenylpyrimidin-5-yl)(phenyl)methanone (**5ab**). Yield = 45% (0.0458 g). White solid. Mp 87.9−89.6 °C. IR (KBr) ν = 2987, 2922, 1655, 1552, 1415, 1182, 921, 742, and 684 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.06 (s, 1H), 8.60−8.55 (m, 2H), 7.79−7.74 (m, 2H), 7.66 (dd, J = 7.5, 2.1 Hz, 2H), 7.63−7.57 (m, 4H), 7.44 (d, J = 7.7 Hz, 2H), 7.40 (dd, J = 7.0, 4.4 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 195.0, 163.8, 163.6, 157.9, 136.9, 136.5, 136.0, 134.0, 131.6, 130.4, 129.6, 129.3, 129.1, 128.9, 128.8, 128.6, 128.3 ppm. HRMS m/z: calcd for $C_{23}H_{17}N_2O$ [M + H]$^+$ 337.1335, found: 337.1345.

4-Methyl-2,6-diphenylpyrimidine (**5ac**) *and* (**5ae**). Yield = 53% (0.0390 g) (**5ac**), 38% (0.0283 g) (**5ae**). White solid. Mp 74.9−75.2 °C. IR (KBr) ν = 2970, 2923, 1570, 1534, 1366, 1028, 747, and 692 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.58−8.50 (m, 2H), 8.38−8.28 (m, 2H), 7.91 (s, 1H), 7.64−7.53 (m, 6H), 2.62 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.2, 163.0, 162.7, 137.4, 136.4, 131.0, 130.7, 129.0, 128.6, 127.8, 127.0, 114.3, 24.1 ppm. HRMS m/z: calcd for $C_{17}H_{15}N_2$ [M + H]$^+$ 247.1230, found: 247.1238.

2,4,6-Triphenylpyrimidine (**5ad**). Yield = 74% (0.0689 g). White solid. Mp 98.2−99.3 °C. IR (KBr) ν = 2987, 2901, 1567, 1359, 1233, 1056, 736, and 679 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.71−8.64 (m, 2H), 8.56 (s, 1H), 8.54−8.48 (m, 4H), 7.67−7.57 (m, 9H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.2, 163.3, 137.5, 136.6, 131.2, 130.9, 129.0, 128.7, 128.0, 127.4, 110.5 ppm. HRMS m/z: calcd for $C_{22}H_{17}N_2$ [M + H]$^+$ 309.1386, found: 309.1395.

4,6-Dimethyl-2-phenylpyrimidine (**5af**). Yield = 36% (0.0199 g). White solid. Mp 74.3−75.4 °C. IR (KBr) ν = 2923, 2852, 1593, 1533, 1364, 1172, 1025, 854, 748, and 692 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.44−8.35 (m, 2H), 7.53−7.48 (m, 3H), 7.19 (s, 1H), 2.49 (s, 6H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.6, 162.6, 137.4, 130.5, 128.5, 127.7, 118.3, 23.7 ppm. HRMS m/z: calcd for $C_{12}H_{13}N_2$ [M + H]$^+$ 185.1073, found: 185.1080.

2-Phenyl-5,6,7,8-tetrahydroquinazoline (**5ag**). Yield = 30% (0.0192 g). White solid. Mp 38.3−40.4 °C. IR (KBr) ν = 2928, 2854, 1573, 1542, 1423, 1395, 1258, 1022, 735, and 691 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.56 (s, 1H), 8.40−8.29 (m, 2H), 7.53−7.45 (m, 3H), 2.86 (t, J = 6.3 Hz, 2H), 2.75 (t, J = 6.2 Hz, 2H), 1.92−1.83 (m, 2H), 1.82−1.75 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.7, 160.6, 157.3, 137.4, 130.2, 128.5, 128.3, 127.4, 31.6, 24.8, 21.8, 21.6 ppm. HRMS m/z: calcd for $C_{14}H_{15}N_2$ [M + H]$^+$ 211.1230, found: 211.1240.

1-(4-Methyl-2-(pyridin-3-yl)pyrimidin-5-yl)ethanone (**5ah**). Yield = 41% (0.0270 g). White solid. Mp 92.7−95.5 °C. IR (KBr) ν = 2924, 2853, 1680, 1566, 1524, 1409, 1272, 1227, 1025, 965, 782, and 710 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.56 (dd, J = 2.3, 0.9 Hz, 1H), 9.33 (s, 1H), 8.77 (dd, J = 4.8, 1.7 Hz, 1H), 8.74−8.69 (m, 1H), 7.63−7.57 (m, 1H), 2.75 (s, 3H), 2.68 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 198.6, 167.1, 162.2, 158.7, 152.1, 149.4, 135.6, 131.8, 128.4, 124.0, 29.4, 24.4 ppm. HRMS m/z: calcd for $C_{12}H_{12}N_3O$ [M + H]$^+$ 214.0975, found: 214.0984.

Ethyl 4-Methyl-2-phenylpyrimidine-5-carboxylate (**5ai**). Yield = 63% (0.0459 g). White solid. Mp 81.5−83.9 °C. IR (KBr) ν = 2975, 2922, 1713, 1562, 1536, 1419, 1360, 1277, 1226, 1075, 768, and 691 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.18 (s, 1H), 8.54−8.42 (m, 2H), 7.64−7.51 (m, 3H), 4.40−4.32 (m, 2H), 2.81 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.1, 164.5, 164.3, 158.9, 136.1, 131.8, 128.8, 128.4, 121.3, 61.3, 24.3, 14.0 ppm. HRMS m/z: calcd for $C_{14}H_{15}N_2O_2$ [M + H]$^+$ 243.1128, found: 243.1132.

Ethyl 2-(4-Bromophenyl)-4-methylpyrimidine-5-carboxylate (**5ci**). Yield = 60% (0.0578 g). White solid. Mp 105.8−107.4 °C. IR (KBr) ν = 2925, 2853, 1721, 1562, 1420, 1279, 1106, 1068, 1008, and 790 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.16 (s, 1H), 8.39−8.33 (m, 2H), 7.79−7.74 (m, 2H), 4.40−4.31 (m, 2H), 2.80 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.3, 164.4, 163.4, 158.9, 135.3, 131.9, 130.3, 125.7, 121.5, 61.4, 24.3, 14.0 ppm. HRMS m/z: calcd for $C_{14}H_{14}BrN_2O_2$ [M + H]$^+$ 321.0233, found: 321.0246.

Ethyl 4-Methyl-2-p-tolylpyrimidine-5-carboxylate (**5fi**). Yield = 61% (0.0446 g). White solid. Mp 62.9−64.0 °C. IR (KBr) ν = 2919, 2852, 1721, 1568, 1425, 1274, 1106, 1078, and 787 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.14 (s, 1H), 8.39−8.31 (m, 2H), 7.36 (d,

J = 8.0 Hz, 2H), 4.39–4.32 (m, 2H), 2.79 (s, 3H), 2.40 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.0, 164.5, 164.4, 158.9, 141.8, 133.5, 129.5, 128.4, 120.9, 61.2, 24.3, 21.1, 14.0 ppm. HRMS m/z: calcd for $C_{15}H_{17}N_2O_2$ $[M + H]^+$ 257.1285, found: 257.1294.

*Ethyl 2-Methylbenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxylate (**5oi**).* Yield = 42% (0.0325 g). White solid. Mp 154.4–157.8 °C. IR (KBr) ν = 2923, 2851, 1714, 1637, 1457, 1263, 1457, 1263, 1077, and 769 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.96 (s, 1H), 8.51–8.47 (m, 1H), 7.87–7.81 (m, 1H), 7.60–7.54 (m, 1H), 7.47–7.42 (m, 1H), 4.43–4.34 (m, 2H), 2.84 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.9, 164.0, 149.2, 144.4, 139.9, 127.4, 126.7, 121.9, 119.2, 113.3, 110.4, 61.2, 26.1, 14.2 ppm. HRMS m/z: calcd for $C_{14}H_{14}N_3O_2$ $[M + H]^+$ 256.1081, found: 256.1091.

*2,5-Diphenylpyrimidine (**5aj**).* Yield = 80% (0.0556 g). White solid. Mp 92.7–94.8. IR (KBr) ν = 2987, 2922, 1535, 1433, 1377, 1072, 1019, 743, and 689 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.26 (s, 2H), 8.51–8.42 (m, 2H), 7.92–7.85 (m, 2H), 7.60–7.53 (m, 5H), 7.52–7.47 (m, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.1, 155.3, 136.8, 133.8, 131.0, 130.9, 129.3, 128.8, 127.6, 126.7 ppm. HRMS m/z: calcd for $C_{16}H_{13}N\ _2$ $[M + H]\ ^+$ 233.1073, found: 233.1082.

*2-(4-Nitrophenyl)-5-phenylpyrimidine (**5hj**).* Yield = 89% (0.0744 g). White solid. Mp 207.1–208.6 °C. IR (KBr) ν = 3062, 3038, 1519, 1430, 1340, 1106, 800, 742, and 689 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.08 (s, 2H), 8.68 (d, J = 8.6 Hz, 2H), 8.35 (d, J = 8.6 Hz, 2H), 7.66 (d, J = 7.4 Hz, 2H), 7.61–7.46 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.4, 155.5, 149.4, 143.2, 134.1, 133.0, 129.7, 129.4, 129.1, 127.1, 124.0 ppm. HRMS m/z: calcd for $C_{16}H_{12}N_3O_2$ $[M + H]^+$ 278.0924, found: 278.0936.

*5-Phenyl-2-(pyridin-3-yl)pyrimidine (**5jj**).* Yield = 72% (0.0504 g). White solid. Mp 147.7–149.8 °C. IR (KBr) ν = 2987, 2901, 1579, 1437, 1375, 1019, 967, 784, and 694 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.57 (s, 1H), 9.31 (s, 2H), 8.77–8.68 (m, 2H), 7.89 (d, J = 7.5 Hz, 2H), 7.64–7.54 (m 3H), 7.54–7.48 (m, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.6, 155.5, 151.5, 148.8, 134.9, 133.6, 132.3, 131.6, 129.3, 129.0, 126.8, 123.9 ppm. HRMS m/z: calcd for $C_{15}H_{12}N_3$ $[M + H]^+$ 234.1026, found: 234.1021.

*N,N-Diphenyl-4′-(4-phenylpyrimidin-2-yl)biphenyl-4-amine (**6**).* Yield = 89% (0.7382 g). Yellow solid. Mp 166.2–168.7 °C. IR (KBr) ν = 2987, 2901, 1580, 1489, 1381, 1278, 1074, 825, 754, and 696 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.97 (d, J = 5.3 Hz, 1H), 8.59 (d, J = 8.0 Hz, 2H), 8.40–8.33 (m, 2H), 8.01 (d, J = 5.3 Hz, 1H), 7.83 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 4.8 Hz, 3H), 7.34 (t, J = 7.6 Hz, 4H), 7.13–7.04 (m, 8H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.1, 162.9, 158.7, 147.2, 146.9, 141.8, 136.2, 135.8, 133.0, 131.3, 129.6, 129.1, 128.4, 127.7, 127.1, 126.3, 124.3, 123.4, 123.0, 114.9 ppm. HRMS m/z: calcd for $C_{34}H_{26}N_3$ $[M + H]^+$ 476.2121, found: 476.2122.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02767.

Reaction procedures and ^{1}H and ^{13}C NMR spectra of all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: xuxp@suda.edu.cn.
*E-mail: shunjun@suda.edu.cn.

ORCID

Shun-Jun Ji: 0000-0002-4299-3528

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the Natural Science Foundation of China (Grants 21372174 and 21672157), the Ph.D. Programs Foundation of Ministry of Education of China (Grant 2013201130004), the Research Grant from the Innovation Project for Graduate Student of Jiangsu Province (Grant KYZZ15_0322), and PAPD and Soochow University for financial support.

■ REFERENCES

(1) (a) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry: Part B: Reactions and Synthesis*; Springer: New York, 2001. (b) Notz, W.; Tanaka, F.; Barbas, C. F., III *Acc. Chem. Res.* **2004**, *37*, 580–591.

(2) (a) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471–5569. (b) Allen, A. E.; MacMillan, D. W. C. *Chem. Sci.* **2012**, *3*, 633–658. (c) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774–7854.

(3) (a) Córdova, A. *Catalytic Asymmetric Conjugate Reactions*; Wiley-VCH: Weinheim, Germany, 2010. (b) Erkkilä, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416–5470. (c) Muller, D.; Alexakis, A. *Chem. Commun.* **2012**, *48*, 12037–12049.

(4) For selected examples of β-functionalization with directing groups, see: (a) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542–9543. (b) Huang, Z.; Dong, G. *Tetrahedron Lett.* **2014**, *55*, 5869–5889. (c) Qiu, G.; Wu, J. *Org. Chem. Front.* **2015**, *2*, 169–178. (d) Zhang, F.-L.; Hong, K.; Li, T.-J.; Park, H.; Yu, J.-Q. *Science* **2016**, *351*, 252–256. (e) Yang, K.; Li, Q.; Liu, Y.; Li, G.; Ge, H. *J. Am. Chem. Soc.* **2016**, *138*, 12775–12778.

(5) For selected examples of β-functionalization via saturated carbonyls, see: (a) Renaudat, A.; Jean-Gérard, L.; Jazzar, R.; Kefalidis, C. E.; Clot, E.; Baudoin, O. *Angew. Chem., Int. Ed.* **2010**, *49*, 7261–7265. (b) Zhou, J.; Wu, G.; Zhang, M.; Jie, X.; Su, W. *Chem. - Eur. J.* **2012**, *18*, 8032–8036. (c) Moon, Y.; Kwon, D.; Hong, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 11333–11336. (d) Leskinen, M. V.; Yip, K.-T.; Valkonen, A.; Pihko, P. M. *J. Am. Chem. Soc.* **2012**, *134*, 5750–5753. (e) Huang, Z.; Dong, G. *J. Am. Chem. Soc.* **2013**, *135*, 17747–17750. (f) Shang, Y.; Jie, X.; Zhou, J.; Hu, P.; Huang, S.; Su, W. *Angew. Chem., Int. Ed.* **2013**, *52*, 1299–1303. (g) Ueno, S.; Shimizu, R.; Kuwano, R. *Angew. Chem., Int. Ed.* **2009**, *48*, 4543–4545. (h) Jie, X.; Shang, Y.; Zhang, X.; Su, W. *J. Am. Chem. Soc.* **2016**, *138*, 5623–5633.

(6) (a) Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D. W. C. *Science* **2013**, *339*, 1593–1596. (b) Petronijević, F. R.; Nappi, M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2013**, *135*, 18323–18326. (c) Terrett, J. A.; Clift, M. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2014**, *136*, 6858–6861. (d) Jeffrey, J. L.; Petronijević, F. R.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2015**, *137*, 8404–8407.

(7) (a) Zhu, J.; Liu, J.; Ma, R.; Xie, H.; Li, J.; Jiang, H.; Wang, W. *Adv. Synth. Catal.* **2009**, *351*, 1229–1232. (b) Hayashi, Y.; Itoh, T.; Ishikawa, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 3920–3924. (c) Zhang, S.-L.; Xie, H.-X.; Zhu, J.; Li, H.; Zhang, X.-S.; Li, J.; Wang, W. *Nat. Commun.* **2011**, *2*, 211–211. (d) Zhao, Y.-L.; Wang, Y.; Hu, X.-Q.; Xu, P.-F. *Chem. Commun.* **2013**, *49*, 7555–7557.

(8) For selected examples of important pyrimidine derivatives, see: (a) Agarwal, A.; Srivastava, K.; Puri, S. K.; Chauhan, P. M. S. *Bioorg. Med. Chem.* **2005**, *13*, 4645–4650. (b) Lee, S.; Lim, D.; Lee, E.; Lee, N.; Lee, H.; Cechetto, J.; Liuzzi, M.; Freitas-Junior, L. H.; Song, J. S.; Bae, M. A.; Oh, S.; Ayong, L.; Park, S. B. *J. Med. Chem.* **2014**, *57*, 7425–7434. (c) Itami, K.; Yamazaki, D.; Yoshida, J. *J. Am. Chem. Soc.* **2004**, *126*, 15396–15397. (d) Aizawa, N.; Pu, Y.-J.; Sasabe, H.; Kido, J. *Org. Electron.* **2012**, *13*, 2235–2242. (e) Li, L.; Ge, J.; Wu, H.; Xu, Q.-H.; Yao, S. Q. *J. Am. Chem. Soc.* **2012**, *134*, 12157–12167. (f) Kato, S.; Yamada, Y.; Hiyoshi, H.; Umezu, K.; Nakamura, Y. *J. Org. Chem.* **2015**, *80*, 9076–9090.

(9) (a) Wang, L.; Xiao, J.; Loh, T.-P. *ChemCatChem* **2014**, *6*, 1183–1185. (b) Turlik, A.; Chen, Y.; Newhouse, T. R. *Synlett* **2016**, *27*, 331–336. (c) Stahl, S. S.; Diao, T. *Comp. Org. Synth.* **2014**, *7*, 178–212.

(10) (a) Ananchenko, G. S.; Fischer, H. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 3604−3621. (b) Ananchenko, G.; Marque, S.; Gigmes, D.; Bertin, D.; Tordo, P. *Org. Biomol. Chem.* **2004**, *2*, 709−715. (c) Hu, X.-Q.; Qi, X.; Chen, J.-R.; Zhao, Q.-Q.; Wei, Q.; Lan, Y.; Xiao, W.-J. *Nat. Commun.* **2016**, *7*, 11188−11199.

(11) (a) Sibi, M. P.; Hasegawa, M. *J. Am. Chem. Soc.* **2007**, *129*, 4124. (b) Van Humbeck, J. F.; Simonovich, S. P.; Knowles, R. R.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 10012−10014. (c) Akagawa, K.; Fujiwara, T.; Sakamoto, S.; Kudo, K. *Org. Lett.* **2010**, *12*, 1804−1807.

(12) For selected examples of TEMPO-Fe complexation, see: (a) Ahlers, C.; Dickman, M. H. *Inorg. Chem.* **1998**, *37*, 6337−6340. (b) Wang, N.; Liu, R.; Chen, J.; Liang, X. *Chem. Commun.* **2005**, 5322−5324. (c) Smith, J. M.; Mayberry, D. E.; Margarit, C. G.; Sutter, J.; Wang, H.; Meyer, K.; Bontchev, R. P. *J. Am. Chem. Soc.* **2012**, *134*, 6516−6519. (d) Scepaniak, J. J.; Wright, A. M.; Lewis, R. A.; Wu, G.; Hayton, T. W. *J. Am. Chem. Soc.* **2012**, *134*, 19350−19353. (e) Ma, S.; Liu, J. X.; Li, S. H.; Chen, B.; Cheng, J. J.; Kuang, J. Q.; Liu, Y.; Wan, B. Q.; Wang, Y. L.; Ye, J. T.; Yu, Q.; Yuan, W. M.; Yu, S. C. *Adv. Synth. Catal.* **2011**, *353*, 1005−1017. (f) Jiang, X.; Zhang, J.; Ma, S. *J. Am. Chem. Soc.* **2016**, *138*, 8344−8347.

(13) (a) Koike, T.; Akita, M. *Chem. Lett.* **2009**, *38*, 166−167. (b) Bui, N.-N.; Ho, X.-H.; Mho, S.-I.; Jang, H.-Y. *Eur. J. Org. Chem.* **2009**, *2009*, 5309−5312. (c) Pouliot, M.; Renaud, P.; Schenk, K.; Studer, A.; Vogler, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 6037−6040. (d) Kano, T.; Mii, H.; Maruoka, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 6638−6641. (e) Kafka, F.; Holan, M.; Hidasová, D.; Pohl, R.; Císařová, I.; Klepetářová, B.; Jahn, U. *Angew. Chem., Int. Ed.* **2014**, *53*, 9944−9948.

(14) For selected recent reviews of Fe catalyst, see: (a) Gopalaiah, K. *Chem. Rev.* **2013**, *113*, 3248−3296. (b) Jia, F.; Li, Z. *Org. Chem. Front.* **2014**, *1*, 194−214. (c) Bauer, I.; Knölker, H. J. *Chem. Rev.* **2015**, *115*, 3170−3387. (d) Yang, X.-H.; Song, R.-J.; Xie, Y.-X.; Li, J.-H. *ChemCatChem* **2016**, *8*, 2429−2445.

(15) Details of experiments and results are summarized in the Supporting Information.

(16) (a) Sollenberger, P. Y.; Martin, R. B. *J. Am. Chem. Soc.* **1970**, *92*, 4261−4270. (b) Bahmanyar, S.; Houk, K. N. *J. Am. Chem. Soc.* **2001**, *123*, 11273−11283. (c) Nielsen, M.; Worgull, D.; Zweifel, T.; Gschwend, B.; Bertelsen, S.; Jørgensen, K. A. *Chem. Commun.* **2011**, *47*, 632−649.