JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c00007 • Publication Date (Web): 05 Mar 2020

Ruthenium-catalyzed *meta*-selective C_{Ar} – H bond formylation of arenes.

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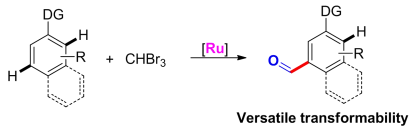
Supporting Information Placeholder



ABSTRACT: The *meta*-C_{Ar}–H bond formylation of arenes has been achieved using $CHBr_3$ as a formyl source in the presence of [Ru(*p*-cym)$(OAc)_2$] as catalyst. This method provides efficient access to the preparation of various *meta*-substituted aromatic compounds, such as alcohols, ethers, amines, nitriles, alkenes, halogens, carboxylic acids, and their derivatives, through transformation of the versatile formyl group. Furthermore, mechanism studies show that the key active species is a pentagonal ruthenacycle complex.

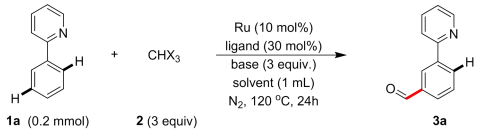
Aromatic aldehydes are essential compounds, with their versatile formyl groups employed for further transformations into various other functional groups, such as alcohols, carboxylic acids, amines, nitriles, and halogens, that are widely present in bioactive natural molecules, pharmaceuticals, agrochemicals, and many functional materials.[1] To date, numerous methods for the synthesis of aromatic aldehydes have been reported. The most efficient methods involve direct installation of a formyl group on the aromatic ring. Conventional electrophilic aromatic formylations, such as the Gattermann–Koch reaction,[2] Duff reaction,[3] Reimer–Tiemann reaction,[4] Rieche formylation,[5] and Vilsmeier–Haack reaction,[6] are perfectly suited to this goal, avoiding prefunctionalization before formylation. However, these transformations are not suitable for electron-deficient aromatic substrates. Furthermore, the functional group tolerance is low. With the development of transition-metal (TM)-catalyzed C-H bond functionalization in recent years, aromatic aldehydes have been efficiently obtained by directing-group-assisted C_{Ar}–H formylation in the presence of TMs.[7] However, regardless of whether electrophilic aromatic formylation or TM-catalyzed aromatic C – H bond formylation is used, these methods are limited to formylation at the *ortho/para*-position relative to substituents. Accordingly, the efficient *meta*-C_{Ar}–H formylation of arenes remains challenging.

In recent years, various TM-catalyzed *meta*-C_{Ar} – H bond functionalizations have been achieved in the literature using alternative strategies.[8] Ruthenium complexes are inexpensive, highly active, and distinctive catalysts that can not only catalyze *ortho*-C_{Ar}–H bond activation,[9] but also *meta*-C_{Ar} – H bond activation through the Ru – C_{Ar} bond *ortho/para*-directing effect.[10] Herein, we have achieved the *meta*-C_{Ar}–H bond formylation of arenes using $CHBr_3$ as the formyl source in the present of a ruthenium catalyst.

Initially, we selected readily available 2-phenylpyridine and $CHBr_3$ as representative reactants to explore favorable conditions for the *meta*-C_{Ar}–H bond formylation of arenes catalyzed by a ruthenium complex. The transformation was conducted in a thick-walled Schlenk reaction tube at 120 ℃ for 24 h under an inert atmosphere (N_2 gas), as shown in Table 1. The target product was provided in 16% yield in acetonitrile when [Ru(*p*-cym)$(OAc)_2$], prepared in our laboratory, and common K_2CO_3 were employed as catalyst and base, respectively (Table 1, entry 1). Usually, carboxylic acids are popular and efficient promoters of Ru-catalyzed C_{Ar} – H bond activation.[10d] Carboxylic acid screening showed that the formylation process was

promoted by Ac-Leu-OH, providing the desired product in a 53% isolated yield (entry 2). Other carboxylic acids, such as 2,4,6-trimethylbenzoic acid and 1-adamantane carboxylic acid, showed inferior performance (entries 3 and 4). Formylation also proceeded in 1,4-dioxane and THF as solvents, but lower yields were obtained (entries 5 and 6). No products were obtained in toluene and DMF (entries 7 and 8). Na_2CO_3, KOAc, and Cs_2CO_3 were also tested as bases in the formylation. The results

Table 1. Condition Optimization of the Ru-Catalyzed *meta*-C_{Ar}–H Formylation

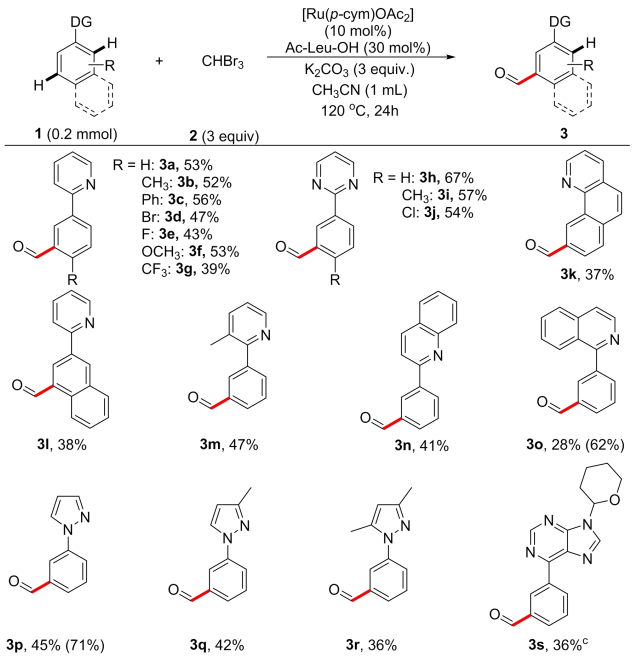


Entry	formyl source	catalyst	base	ligand	solvent	yield (%)
1	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	—	CH_3CN	16
2	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	Ac-Leu-OH	CH_3CN	53
3	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	MesCOOH	CH_3CN	8
4	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	1-AdCOOH	CH_3CN	14
5	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	Ac-Leu-OH	1,4-Dioxane	28
6	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	Ac-Leu-OH	THF	18
7	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	Ac-Leu-OH	toluene	0
8	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	Ac-Leu-OH	DMF	0
9	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	Na_2CO_3	Ac-Leu-OH	CH_3CN	0
10	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	KOAc	Ac-Leu-OH	CH_3CN	11
11	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	Cs_2CO_3	Ac-Leu-OH	CH_3CN	26
12	CHI_3	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	Ac-Leu-OH	CH_3CN	51
13	$CHCl_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	Ac-Leu-OH	CH_3CN	21
14	$CHBr_3$	[Ru(*p*-cym)$(OAc)_2$]	K_2CO_3	Ac-Leu-OH	CH_3CN	32
15	$CHBr_3$	$RuCl_3$	K_2CO_3	Ac-Leu-OH	CH_3CN	19
16	$CHBr_3$	$Ru_3(CO)_{12}$	K_2CO_3	Ac-Leu-OH	CH_3CN	0
17	$CHBr_3$	$Pd(OAc)_2$	K_2CO_3	Ac-Leu-OH	CH_3CN	0
18	$CHBr_3$	—	K_2CO_3	Ac-Leu-OH	CH_3CN	0

showed that the Na_2CO_3 was not compatible (Table 1, entry 9), while KOAc and Cs_2CO_3 were effective, but gave poor yields (entries 10 and 11). An examination of other formylation reagents showed that CHI_3 also provided the target product in 51% yield (entry 12), while $CHCl_3$ showed low efficiency (entry 13). [Ru(*p*-cym)$Cl_2]_2$ and $RuCl_3$ were also efficient catalysts for C – H bond formylation (entries 14 and 15), although the yields were inferior to those obtained using [Ru(*p*-cym)$(OAc)_2$]. When $Ru_3(CO)_{12}$, $Pd(OAc)_2$, and no transition metal were employed as catalysts in the process, no desired product was obtained (entries 16–18).

Under the optimized conditions, the generality of *meta*-C_{Ar} – H bond formylation catalyzed by the ruthenium complex was investigated using various 2-phenylpyridine derivatives as substrates, as shown in Scheme 1. Initially, several 2-phenylpyridines bearing various groups on the phenyl ring were employed as reactants. 2-Phenylpyridines bearing alkyl or aryl groups reacted successfully, providing the target products in moderate yields (**3b**, **3c**, **3i**). Halogen substituents were also compatible with the transformation, offering potential active sites for further functionalization (**3d, 3e, 3j**). The electronic nature of the phenyl ring was also found to influence the transformation efficiency. An electron-donating substituent (–OCH_3, **3f**) on the phenyl ring was more favorable for formylation than an electron-withdrawing (– CF_3, **3g**) functional group. When 7,8-benzoquinoline and 2-(2-naphthyl)pyridine were used as substrates, the corresponding products were successfully obtained (**3k**, **3l**). An investigation of nitrogen-containing chelating groups showed that pyrimidine was a leading directing group, with good isolated yields obtained (**3h–j**). The desired products were also obtained when pyridines bearing a methyl group (**3m**), quinoline (**3n**), isoquinoline (**3o**), and pyrazole (**3p–r**) were used as directing groups. Notably, the ruthenium-catalyzed *meta*-C_{Ar}–H formylation was also suitable for phenyl ring *meta*-position modification and the functionalization of 6-phenyl purine nucleobases as bioactive molecule (**3s**).

Scheme 1. Substrate Scope of the *meta*-C_{Ar} – H Formylation Catalyzed by Ruthenium.

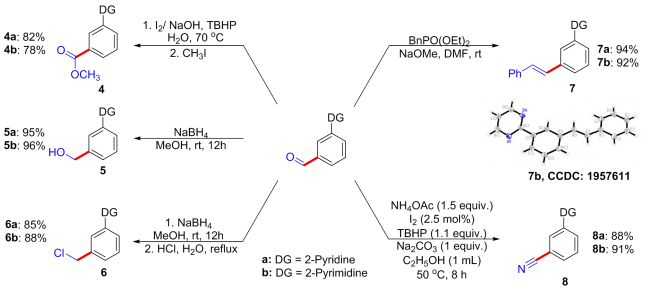


[a] Reaction Conditions: **1** (0.2 mmol), **2** (0.6 mmol), [Ru(*p*-cym)$(OAc)_2$] (10 mol%), Ac-Leu-OH (30 mol%), K_2CO_3 (0.6 mmol), CH_3CN (1 mL), 120 °C, 24 h. isolated yield, [b] yields based on recovered starting material are listed in parentheses. [c] xylene as solvent

To illustrate the versatile synthetic potential of the arylaldehyde products, different transformations were performed, as shown in Scheme 2. For example, carboxylic acid[11] and benzyl alcohol[12] were synthesized from arylaldehyde by a simple redox reaction (4, 5). Benzyl alcohol reacts further with HCl to give benzyl chloride (6).[13] By means of the famous Wittig reaction, the reaction of arylaldehydes with diethyl benzylphosphonate provided olefins in excellent yields (7).[14] The structure of product

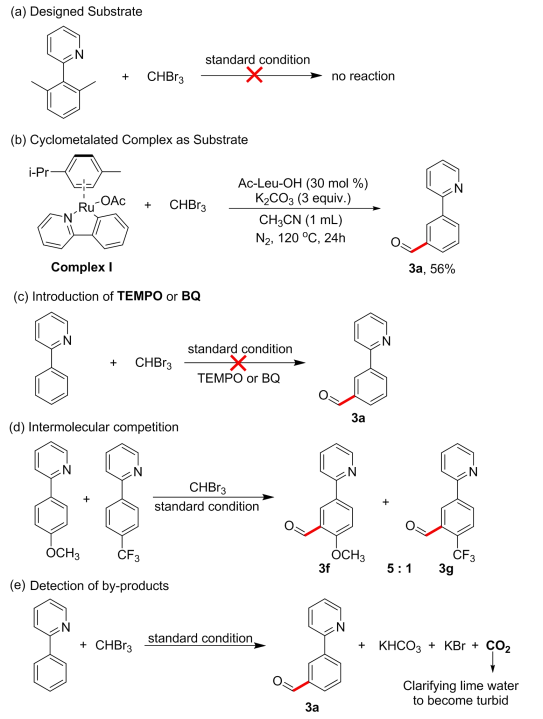
7b was confirmed by single-crystal X-ray diffraction. Furthermore, benzonitrile was obtained by reacting arylaldehydes with ammonium acetate (8).[15]

Scheme 2. Synthetic Utility of the Formylation.



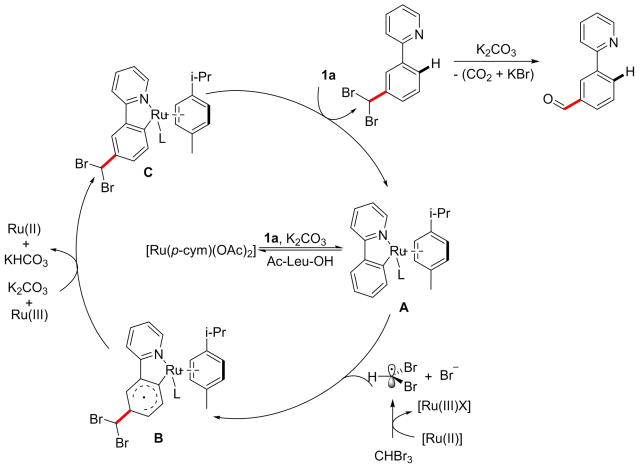
To gain insight into the Ru(II)-catalyzed *meta*-C_{Ar} – H formylation mechanism, some test reactions were performed, as shown in Scheme 4. First, under the optimized conditions, 2-(2,6-dimethylphenyl)pyridine, in which the two *ortho*-positions relative to the directing group were occupied by two methyl groups, did not react with $CHBr_3$ (Scheme 3a).

Scheme 3. Preliminary Mechanistic Probes.



This supported that *ortho*-C_{Ar}–H metalation was necessary in the ruthenium-catalyzed formylation. Next, pentagonal ruthenacycle **I** was prepared by the reaction of 2-phenylpyridine with [Ru(*p*-cym)OAc_2] in CH_2Cl_2 at room temperature for 18 h. This experiment indicated that the *meta*-C_{Ar} – H formylation was promoted by ruthenacycle complex **I** to give product **3a** in 56% isolated yield (Scheme 3b). These results indicated that pentagonal ruthenacycle **I** was a key active species in the formylation process. Furthermore, when radical scavengers, such as TEMPO (2,2,6,6-tetramethylpiperidin-1-yl)oxyl) and BQ (1,4-benzoquinone), were added to the standard reaction, no product was obtained, indicating that the formylation involved a single-electron transfer process (Scheme 3c). Next, to study the impact of electronic properties on the formylation, a scrambling test of 2-(4-methoxyphenyl)pyridine and 2-(4-(trifluoromethyl)phenyl)pyridine, bearing electron-donating (–OCH_3) and electron-withdrawing (–CF_3) groups, respectively, reacted with $CHBr_3$ under the optimized conditions to provide product **3f** predominantly (Scheme 3d). This result indicated that the ruthenium-catalyzed C_{Ar}–H formylation was an electrophilic substitution process. Finally, after the reaction was complete, the gas from the reaction system caused clarified lime water to become turbid, showing that CO_2 was a byproduct of the process (Scheme 3e).

Scheme 4. Proposed Catalytic Mechanism.



From the aforementioned experimental results and literature relating to ruthenium-catalyzed C_{Ar}–H bond activation,[9] a plausible mechanism was proposed for the *meta*-C_{Ar}–H formylation process, as shown in Scheme 4. *Ortho*-C_{Ar}–H bond metalation of 2-phenylpyridine by [Ru(*p*-cym)OAc_2] generates key pentagonal ruthenacycle species **A**. The dibromomethyl radical, formed by a ruthenium-complex-mediated single-electron transfer, attacks active intermediate **A** at the pyridyl *meta*-position, producing intermediate **B**. The deprotonation of active intermediate **B**, aided by ruthenium and K_2CO_3, provides complex **C**. Finally, complex **C** undergoes ligand exchange with 2-phenylpyridine to give the recycled active catalyst species and the *meta*-dibromomethylated product, which further reacts with K_2CO_3 to give the final product, and KBr and CO_2 as byproducts.

In conclusion, we have achieved Ru-catalyzed *meta*-C_{Ar}–H formylation using $CHBr_3$ as the formyl source. Mechanistic

studies showed that a radical intermediate might be involved in this process, and that a pentagonal ruthenacycle was the key active species. This provides an efficient method for the synthesis of various *meta*-substituted aromatic compounds via an active formyl group, and allows further transformation to obtain many other functional groups.

EXPERIMENTAL SECTION

Materials and Methods. All commercial reagents and solvents were used directly without additional purification. Column chromatography were performed on silica gel 200-300 mesh. ^{1}H NMR and ^{13}C NMR spectra were registered on a Bruker AscendTM 400 spectrometer (Germany). Chemical shifts were reported in units (ppm) referenced to 0.0 ppm of TMS in the ^{1}H spectrum and 77.0 ppm of $CDCl_3$ in the ^{13}C spectrum. All coupling constants were reported in Hertz (Hz). HRMS data were obtained using Tof ESI-MS instrument on a Waters LCT PremierxeTM (USA). Crystal (7b) grows in CH_2Cl_2/PE system at room temperature. Single-crystal X-ray crystallography was carried out on a Bruker Smart Apex II diffractometer system. The pyridine derivatives were prepared via Suzuki coupling of the corresponding arylboronic acids and 2-bromopyridine according to literature report.[16]

Typical Experimental Procedure of ruthenium-catalyzed meta-selective C-H bond formylation of Arenes: 2-Phenylpyridine (0.2 mmol), $CHBr_3$ (0.6 mmol, 3.0 equiv.), [Ru(*p*-cymene)$(OAc)_2$], (0.01 mmol, 10 mol %), K_2CO_3 (0.4 mmol, 2.0 equiv), Ac-Leu-OH (30 mmol %), dry acetonitrile (1 mL) were charged into a pre-dried 30-mL pressure tube sealed with rubber plugs under N_2 atmosphere. The reaction mixture was stirred at 120 °C oil bath for 24 h. The reaction was cooled down to room temperature. The mixture was passed through a short pad of celite, washing with a mixture of EtOAc. The organic layer was concentrated under reduced pressure to give a crude oil, which was purified by column chromatography (PE/EtOAc as eluent) on silica gel to afford the desired products.

1 mmol Scale Experimental Procedure of ruthenium-catalyzed meta-selective C-H bond formylation of Arenes: 2-Phenylpyridine or 2-(4-methoxyphenyl)pyridine (1 mmol), $CHBr_3$ (3 mmol, 3.0 equiv.), [Ru(*p*-cymene)$(OAc)_2$], (0.05 mmol, 10 mol %), K_2CO_3 (2 mmol, 2.0 equiv), Ac-Leu-OH (30 mmol %), dry acetonitrile (3 mL) were charged into a pre-dried 75-mL pressure tube sealed with rubber plugs under N_2 atmosphere. The reaction mixture was stirred at 120 ° C oil bath for 36 h. The reaction was cooled down to room temperature. The mixture was passed through a short pad of celite, washing with a mixture of EtOAc. The organic layer was concentrated under reduced pressure to give a crude oil, which was purified by column chromatography (PE/EtOAc as eluent) on silica gel to afford the 3a and 3f products in 42% (76.9 mg) and 48% (102.3 mg) isolated yields respectively.

Preparation of [Ru(*p*-cymene)$(OAc)_2$]: [Ru(*p*-cymene)$(OAc)_2$] were prepared from [Ru(*p*-cymene)$Cl_2]_2$ and KOAc according to literature report.[17]

Preparation of Complex I: Complex I were prepared from [Ru(*p*-cymene)$(OAc)_2$] and 2-phenylpyridine according to literature report.[17]

3-(pyridin-2-yl)benzaldehyde (**3a**, colorless oil, PE/EtOAc = 3:1 as eluent, 19.4mg, 53% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.70 (d, *J* = 4.4 Hz, 1H), 8.49 (s, 1H), 8.27 (d, *J* = 7.7 Hz, 1H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.81 – 7.73 (m, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.27 (m, 1H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.2, 155.8, 149.8, 140.3, 137.0 (d), 132.7, 129.7, 129.5, 128.4, 122.8, 120.6. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{10}NO$ 184.0757; Found 184.0752.

2-methyl-5-(pyridin-2-yl)benzaldehyde (**3b**, yellow oil, PE/EtOAc = 3:1 as eluent, 20.5mg, 52% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 8.69 (d, *J* = 4.2 Hz, 1H), 8.42 (s, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 3.6 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.30 – 7.19 (m, 1H), 2.70 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.8, 155.9, 149.8, 141.2, 137.0, 134.4, 132.4, 131.6, 130.7, 122.5, 120.2, 19.5. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{12}NO$ 198.0914; Found 198.0913.

4-(pyridin-2-yl)-[1,1'-biphenyl]-2-carbaldehyde (3c, yellow oil, PE/EtOAc = 3:1 as eluent, 26mg, 56% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.74 (d, *J* = 4.2 Hz, 1H), 8.60 (d, *J* = 1.4 Hz, 1H), 8.45 – 8.34 (m, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.48 (m, 5H), 7.33 – 7.25 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.3, 155.9, 149.9, 146.3, 138.9, 137.4, 137.0, 133.9, 131.9, 131.5, 130.1, 128.5, 128.3, 125.8, 122.7, 120.6. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{18}H_{14}NO$ 260.1070; Found 260.1075.

2-bromo-5-(pyridin-2-yl)benzaldehyde (**3d**, white solid, PE/EtOAc = 3:1 as eluent, 24.4mg, 47% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.44 (s, 1H), 8.72 (d, *J* = 4.7 Hz, 1H), 8.49 (d, *J* = 2.2 Hz, 1H), 8.22 (m, 1H), 7.80 (m, 3H), 7.31 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 191.6, 155.0, 149.9, 139.3, 137.1, 134.4, 133.6, 127.9, 127.6, 123.0, 120.4. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{12}H_9BrNO$ 261.9863; Found 261.9861.

2-fluoro-5-(pyridin-2-yl)benzaldehyde (**3e**, white solid, PE/EtOAc = 3:1 as eluent, 17.3mg, 43% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (s, 1H), 8.70 (d, *J* = 4.8 Hz, 1H), 8.45 (m, 1H), 8.36 (m, 1H), 7.82 – 7.74 (m, 2H), 7.31 – 7.25 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 187.0 (d), 166.4, 163.8, 155.1, 149.8, 137.0, 134.9 (d), 127.0 (d), 122.7, 120.3, 117.2, 117.0. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{12}H_9FNO$ 202.0663; Found 202.0667.

2-methoxy-5-(pyridin-2-yl)benzaldehyde (**3f**, white solid, PE/EtOAc = 3:1 as eluent, 22.6mg, 53% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.53 (s, 1H), 8.67 (d, *J* = 4.7 Hz, 1H), 8.41 (d, *J* = 2.4 Hz, 1H), 8.36 (m, 1H), 7.79 – 7.72 (m, 2H), 7.23 (d, *J* = 3.9 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 1H), 4.01 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.6, 162.4, 155.9, 149.6, 136.9, 134.5, 132.1, 126.8, 124.7, 122.0, 119.9, 112.1, 55.9. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{13}H_{12}NO_2$ 214.0863; Found 214.0867.

5-(pyridin-2-yl)-2-(trifluoromethyl)benzaldehyde (**3g**, white solid, PE/EtOAc = 3:1 as eluent, 19.6mg, 39% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (d, *J* = 2.0 Hz, 1H), 8.79 – 8.68 (m, 2H), 8.44 (d, *J* = 8.1 Hz, 1H), 7.94 – 7.83 (m, 3H), 7.35 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 188.8, 154.5, 150.1, 143.30, 137.2, 134.1, 131.8, 127.3, 126.8, 125.0, 123.6, 121.0. HRMS

(ESI) m/z: [M+H]+ Calcd for $C_{13}H_9F_3NO$ 252.0631; Found 252.0632.

3-(pyrimidin-2-yl)benzaldehyde (**3h**, white solid, PE/EtOAc = 3:1 as eluent, 24.7mg, 67% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.14 (s, 1H), 8.96 (s, 1H), 8.84 (d, *J* = 4.3 Hz, 2H), 8.72 (d, J = 7.6 Hz, 1H), 8.02 (d, *J* = 7.3 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.26 (t, *J* = 4.6 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.2, 163.4, 157.4, 138.6, 136.9, 133.9, 130.6 (d), 129.4, 119.7. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{11}H_9N_2O$ 185.0710; Found 185.0712.

2-methyl-5-(pyrimidin-2-yl)benzaldehyde (**3i**, white solid, PE/EtOAc = 3:1 as eluent, 22.6mg, 57% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 8.92 – 8.74 (m, 3H), 8.54 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.21 (d, *J* = 4.8 Hz, 1H), 2.73 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 193.0, 163.5, 157.3, 143.1, 136.0, 134.5, 133.0, 132.7, 132.3, 119.4, 20.0. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{12}H_{11}N_2O$ 199.0866; Found 199.0867.

2-chloro-5-(pyrimidin-2-yl)benzaldehyde (**3j**, white solid, PE/EtOAc = 3:1 as eluent, 23.5mg, 54% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.55 (s, 1H), 9.03 (d, *J* = 1.9 Hz, 1H), 8.84 (d, *J* = 4.8 Hz, 2H), 8.63 (m, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.27 (d, *J* = 4.4 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.4, 162.8, 157.4, 139.8, 137.1, 134.2, 132.6, 130.9, 129.5, 119.8. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{11}H_8ClN_2O$ 219.0320; Found 219.0322.

benzo[h]quinoline-9-carbaldehyde (**3k**, white solid, PE/EtOAc = 3:1 as eluent, 15.3mg, 37% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (s, 1H), 9.79 (s, 1H), 9.08 (m, 1H), 8.23 (m, 2H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.87 (s, 2H), 7.61 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.5, 149.7, 136.1, 146.5, 137.3, 134.9, 131.4, 130.6, 128. 8 (d), 127.2, 126.7, 125.3, 122.5. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{14}H_{10}NO$ 208.0757; Found 208.0757.

3-(pyridin-2-yl)-1-naphthaldehyde (**3l**, 35 mg, colorless oil, PE/EtOAc = 3:1 as eluent, 17.7mg, 38% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.53 (s, 1H), 9.29 (d, *J* = 8.5 Hz, 1H), 8.80 (d, *J* = 4.0 Hz, 1H), 8.76 – 8.69 (m, 2H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.87 (m, 1H), 7.76 – 7.69 (m, 1H), 7.64 (m, 1H), 7.36 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 193.7, 155.6, 150.0, 137.1, 135.6 (d), 134.1, 132.8, 132.0, 129.6, 129.2, 127.4, 125.0, 122.8, 120.5. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{16}H_{12}NO$ 234.0914; Found 234.0913.

3-(3-methylpyridin-2-yl)benzaldehyde (**3m**, yellow oil, PE/EtOAc = 3:1 as eluent, 18.5mg, 47% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.56 (d, *J* = 4.4 Hz, 1H), 8.08 (s, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 2H), 7.25 (m, 1H), 2.39 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.1, 157.1, 147.3, 141.6, 138.8, 136.4, 135.0, 130.9, 130.6, 129.0, 122.7, 20.0. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{13}H_{12}NO$ 198.0914; Found 198.0918.

3-(quinolin-2-yl)benzaldehyde (**3n**, white solid, PE/EtOAc = 3:1 as eluent, 19.1mg, 41% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H), 8.70 (s, 1H), 8.53 – 8.46 (m, 1H), 8.29 (d, *J* = 8.6 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.58 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.2, 155.7, 148.3, 140.6, 137.1, 133.3, 130.3, 129.6, 129.0, 127.5, 126.8, 118.6. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{16}H_{12}NO$ 234.0914; Found 234.0916.

3-(isoquinolin-1-yl)benzaldehyde (**3o**, yellow solid, PE/EtOAc = 3:1 as eluent, 13mg, 28% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.14 (s, 1H), 8.65 (d, *J* = 5.6 Hz, 1H), 8.24 (s, 1H), 8.03 (t, *J* = 12.4 Hz, 3H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.77 – 7.70 (m, 3H), 7.59 (t, *J* = 7.3 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.0, 159.1, 142.3, 140.6, 136.9, 136.5, 135.8, 131.6, 130.3, 129.5, 129.2, 127.7, 127.2, 126.9, 126.5, 120.6. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{16}H_{12}NO$ 234.0914; Found 234.0915.

3-(1H-pyrazol-1-yl)benzaldehyde (**3p**, yellow oil, PE/EtOAc = 3:1 as eluent, 15.6mg, 45% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 8.20 (s, 1H), 8.06 – 8.01 (m, 2H), 7.83 – 7.75 (m, 2H), 7.64 (t, *J* = 7.8 Hz, 1H), 6.58 – 6.49 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 191.4, 141.7, 137.5, 130.3, 127.6, 126.8, 124.7, 119.1, 118.8, 108.3. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{10}H_9N_2O$ 173.0710; Found 173.0709.

3-(3-methyl-1H-pyrazol-1-yl)benzaldehyde (**3q**, white solid, PE/EtOAc = 3:1 as eluent, 15.6mg, 42% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.15 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.91 (d, *J* = 2.2 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 6.31 (d, *J* = 2.1 Hz, 1H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 191.5, 151.3, 140.9, 137.5, 130.2, 127.3, 127.0, 124.2, 118.8, 108.4, 13.7. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{11}H_{11}N_2O$ 187.0866; Found 187.0860.

3-(3,5-dimethyl-1H-pyrazol-1-yl)benzaldehyde (**3r**, yellow oil, PE/EtOAc = 3:1 as eluent, 14.4mg, 36% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.94 (d, *J* = 1.6 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 6.01 (s, 1H), 2.34 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 149.7, 140.8, 139.5, 137.2, 129.9 (d), 127.9, 124.9, 107.8, 13.4, 12.5. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{12}H_{13}N_2O$ 201.1023; Found 201.1022.

3-(9-(tetrahydro-2H-pyran-2-yl)-9H-purin-6-yl)benzaldehyde (**3s**, white solid, PE/EtOAc = 3:1 as eluent, 22.2mg, 36% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 9.33 (s, 1H), 9.13 (d, J = 7.8 Hz, 1H), 9.07 (s, 1H), 8.39 (s, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.74 (t, *J* = 7.7 Hz, 1H), 5.89 (m, 1H), 4.23 (d, *J* = 10.6 Hz, 1H), 3.85 (m, 1H), 2.22 (d, *J* = 12.4 Hz, 1H), 2.14 (d, *J* = 10.1 Hz, 2H), 1.82 (m, 2H), 1.71 (d, *J* = 9.9 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 192.1, 153.2, 152.4, 151.5, 142.6, 136.8 (d), 135.6, 132.2, 131.3, 130.6, 129.4, 82.1, 68.9, 31.9, 24.9, 22.8. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{17}H_{17}N_4O_2$ 309.1347; Found 309.1348.

methyl 3-(pyridin-2-yl)benzoate (**4a**, yellow oil, PE/EtOAc = 3:1 as eluent, 87 mg, 82% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.68 (m, 1H), 8.64 (d, *J* = 1.5 Hz, 1H), 8.23 (m, 1H), 8.12 – 8.05 (m, 1H), 7.80 – 7.74 (m, 2H), 7.55 (m, 1H), 7.28 – 7.21 (m, 1H), 3.94 (d, J = 1.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.9, 156.3, 149.8, 139.7, 136.9, 131.3, 130.7, 130.0, 128.9, 128.0, 122.6, 120.6, 52.2. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{13}H_{12}NO_2$ 214.0863; Found 214.0859.

methyl 3-(pyrimidin-2-yl)benzoate (**4b**, white solid, PE/EtOAc = 3:1 as eluent, 83mg, 78% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (t, *J* = 1.4 Hz, 1H), 8.78 (d, J = 4.8 Hz, 2H), 8.66 – 8.57 (m, 1H), 8.17 – 8.08 (m, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 4.8 Hz, 1H), 3.93 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.8, 163.8, 157.3, 138.0, 132.4, 131.7, 130.7, 129.3, 128.7, 119.5, 52.1. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{12}H_{11}N_2O_2$ 215.0816; Found 215.0825.

(3-(pyridin-2-yl)phenyl)methanol (**5a**, colorless oil, PE/EtOAc = 2:1 as eluent, 88mg, 95% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.5 Hz, 1H), 7.97 (s, 1H), 7.87 (d, *J* = 7.4 Hz, 1H), 7.74 (m, 2H), 7.49 – 7.38 (m, 2H), 7.31 – 7.19 (m, 1H), 4.75 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.3, 149.5, 141.7, 139.5, 136.9, 128.9, 127.5, 126.1, 125.5, 122.2, 120.8, 65.1. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{12}H_{12}NO$ 186.0914; Found 186.0911.

(3-(pyrimidin-2-yl)phenyl)methanol (**5b**, colorless oil, PE/EtOAc = 2:1 as eluent, 96mg, 96% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, *J* = 4.8 Hz, 2H), 8.44 (s, 1H), 8.38 (d, *J* = 6.9 Hz, 1H), 7.53 (s, 2H), 7.21 (s, 1H), 4.81 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 164.5, 157.2, 141.7, 137.5, 129.4, 128.8, 127.2, 126.6, 119.1, 64.7. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{11}H_{11}N_2O$ 187.0866; Found 187.0866.

2-(3-(chloromethyl)phenyl)pyridine (**6a**, colorless oil, PE/EtOAc = 5:1 as eluent, 86mg, 85% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.5 Hz, 1H), 8.07 (s, 1H), 7.99 – 7.90 (m, 1H), 7.80 – 7.72 (m, 2H), 7.48 (d, *J* = 7.1 Hz, 2H), 7.29 – 7.21 (m, 1H), 4.69 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 156.8, 149.7, 139.9, 138.1, 136.8, 129.2 (d), 127.2, 126.9, 122.4, 120.6, 46.2. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{12}H_{11}ClN$ 204.0575; Found 204.0572.

2-(3-(chloromethyl)phenyl)pyrimidine (**6b**, yellow solid, PE/EtOAc = 5:1 as eluent, 90mg, 88% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 4.8 Hz, 2H), 8.50 (s, 1H), 8.43 (d, *J* = 7.3 Hz, 1H), 7.53 (m, 2H), 7.22 (s, 1H), 4.70 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 164.2, 157.3, 138.0 (d), 130.9, 129.1, 128.3 (d), 119.3, 46.1. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{11}H_{10}ClN_2$ 205.0528; Found 205.0528.

(E)-2-(3-styrylphenyl)pyridine (**7a**, white solid, PE/EtOAc = 6:1 as eluent, 121mg, 94% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.3 Hz, 1H), 8.23 (s, 1H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 12.9 Hz, 2H), 7.59 (t, J = 8.7 Hz, 3H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.4 Hz, 2H), 7.31 (d, *J* = 7.3 Hz, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.3, 149.7, 139.8, 137.9, 137.3, 136.8, 129.2 (d), 128.8, 128.5, 127.8, 127.1, 126.6, 126.2, 125.2, 122.3, 120.7. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{19}H_{16}N$ 258.1278; Found 258.1279.

(E)-2-(3-styrylphenyl)pyrimidine (**7b**, white solid, PE/EtOAc = 6:1 as eluent, 119mg, 92% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, J = 4.8 Hz, 2H), 8.65 (s, 1H), 8.38 (d, *J* = 7.7 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.4 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 7.30 (d, J = 7.1 Hz, 1H), 7.26 (d, *J* = 6.4 Hz, 2H), 7.22 (t, *J* = 4.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 164.6, 157.3, 137.9 (d), 137.3, 129.2, 129.0, 128.9, 128.7, 128.4, 127.7, 127.4, 126.6, 126.2, 119.2. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{18}H_{15}N_2$ 259.1230; Found 259.1233.

3-(pyridin-2-yl)benzonitrile (**8a**, white solid, PE/EtOAc = 3:1 as eluent, 79mg, 88% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.33 (s, 1H), 8.24 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 7.4 Hz, 1H), 7.72 (m, 2H), 7.62 – 7.53 (m, 1H), 7.36 – 7.22 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 154.9, 150.0, 140.5, 137.1, 132.2, 131.0, 130.6, 129.6, 123.2, 120.5, 118.7, 113.0. HRMS (ESI) m/z: [M+H]+ Calcd. For $C_{12}H_9N_2$ 181.0761; Found 181.0760.

3-(pyrimidin-2-yl)benzonitrile (**8b**, white solid, PE/EtOAc = 3:1 as eluent, 91mg, 82% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 4.8 Hz, 2H), 8.81 (s, 1H), 8.71 (d, *J* = 7.9 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 4.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.6, 157.5, 138.8, 133.5, 132.2, 132.0, 129.4, 120.0, 118.7, 112.9. HRMS (ESI) m/z: [M+H]+ Calcd for $C_{11}H_8N_3$ 182.0713; Found 182.0712.

Complex **I** (yellow solid, EtOAc/ EtOH = 5:1 as eluent, 326mg, 68% yield): ^{1}H NMR (400 MHz, CDCl3) δ 9.75 (m, ^{1}H), 8.65 (m, 1H), 8.33 (d, *J* = 7.1 Hz, 1H), 8.00 (m, 1H), 7.32 – 7.23 (m, 2H), 7.15 – 7.06 (m, 1H), 7.05 – 6.95 (m, 1H), 5.70 (m, 2H), 5.48 (d, *J* = 5.8 Hz, 1H), 5.25 (d, *J* = 5.6 Hz, 1H), 2.22 (m, 1H), 1.92 (s, 3H), 1.68 (s, 3H), 0.89 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, CDCl3) δ 181.3, 178.9, 172.7, 163.6, 157.1, 142.0, 139.0, 131.0, 127.2, 123.2, 116.5, 100.5, 97.1, 90.1, 89.4, 86.5, 82.5, 31.0, 24.3, 22.3 (d), 18.7.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:. Experimental procedures, characterization data, NMR spectra of products, and crystal structure (PDF).

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We gratefully acknowledge the Program of Science and Technology Innovation Talents of Henan Province(19HASTIT035), the National Natural Science Foundation of China (NSFC, No. 21102005) for financial support of this work.

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