Note

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Overcoming Electron-Withdrawing and Product-Inhibition Effects by Organocatalytic Aerobic Oxidation of Alkyl Pyridines and Related Alkylheteroarenes to Ketones

Hua Wang,[†] Jie Liu,[†] Jian-Ping Qu,[‡]* and Yan-Biao Kang[†]*

[†] Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, China

[‡] Institute of Advanced Synthesis, School of Chemistry and Molecular Engineering, Nanjing Tech University, Nanjing 211816, China

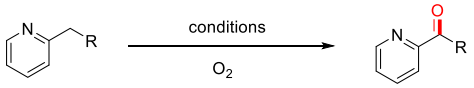
ABSTRACT: An organocatalyzed aerobic benzylic C-H oxidation of alkyl- and aryl heterocycles has been developed. This transition metal-free method is able to overcome the electron-withdrawing effect as well as product-inhibition effects in heterobenzylic radical oxidation. A variety of ketones bearing *N*-heterocyclic groups could be prepared under relatively mild conditions with moderate to high yields.

Ketones bearing *N*-heterocyclic groups are important moieties frequently found in natural products, bioactive reagents as well as agrochemicals and useful intermediates in the synthesis of pharmaceuticals, such as antihistamines and acrivastine. The preparation of such compounds normally involves organometallic reagents. For example, the Friedel-Crafts acylation for the synthesis of acylarenes is not feasible for electron-deficient heterocycles, and 2-acetylpyridine is prepared by acylation of 2-bromopyridine via the Grignard reagent. Another method to prepare ketones bearing electron-deficient heterocycles is to use heterobenzylic C-H oxidation from corresponding alkyl heterocycles. On the other hand, the use of molecular oxygen as a green and sustainable oxidant has attracted considerable attention due to its highly atom-economical, abundant, and environmentally friendly characteristics.[1] Considering that alkyl- and aryl heterocycles are relatively readily available starting materials, the synthesis of *N*-heterocyclic ketones by catalytic aerobic oxidation of alpha-C-H bond under environment-friendly conditions would provide a good alternative. [2-9] However, the utilization of metals as catalysts in aerobic oxidation often suffers product-inhibition by the chelation of heterocycle and newly formed carbonyl to metal-catalysts, resulting in the usages of additives or special treatments. For example, Maes and co-workers developed a base metal (copper and iron) catalyzed oxidation of benzyl pyridine via an acid-promoted imine-enamine tautomerization.[3a] It works effectively with 2- and 4-benzyl pyridine albeit incompetently with 3-benzyl pyridine and 2-methyl pyridine (Scheme 1a). Gao et al. reported an iodide-promoted aerobic oxidation, in which the heterocycles are activated by acetic acid, but only limited to of 2- or 4-benzyl pyridines.[4] Lei et al. found that one equivalent of chloroacetate can promote the aerobic oxidation of heterobenzylic methylenes by forming pyridium salts in the presence of copper catalyst and DMF at 130 °C.[5] This method can be used for both aliphatic and aromatic substituted 2-methylpyridines.

Besides, the oxygenation of C–H bonds on benzylic positions which are directly adjacent to an alkyl group is even more challenging. For example, Stahl et al. investigated the aerobic oxygenation of (hetero)arenes via a cobalt(II)/*N*-hydroxyphthalimide (NHPI) catalysis, they found the electrochemical oxidation was necessary for higher yield.[6]

Scheme 1. Catalytic Aerobic Oxidation of Heterobenzylic Methylenes

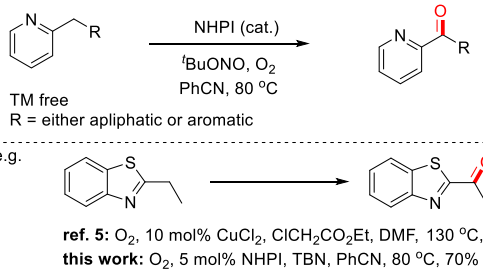
(a) Inorganic salt-catalyzed aerobic benzylic oxidation of 2-alkylpyridines



Conditions	R = Et (non-activated)	R = Ph (activated)	ref.
Fe/Cu (cat.), AcOH (1 equiv), 100 °C	-	80-81%	ref 3
H_4NI (cat.), AcOH (cat.), no solvent, 100 °C	-	92%	ref 4
$CuCl_2$ (cat.), $ClCH_2CO_2Et$ (1 equiv), DMF, 130 °C	78%	92%	ref 5
Co (cat.), NHPI (20 mol%), BuOAc, 90-100 °C	48%	93%	ref 6
E-Chem (RVC|Pt), NHPI (20 mol%), 50 °C	82%	-	ref 6,7
$Fe(BF_4)_2$ (cat.), KTp, HOAt, PhCN, 90 °C, 18 h	25%	-	ref 8

(KTp = potassium tri(1-pyrazolyl)borohydride. HOAt = 1-Hydroxy-7-azabenzotriazole)

(b) Organocatalyzed aerobic benzylic oxidation of 2-alkylpyridines (this work)



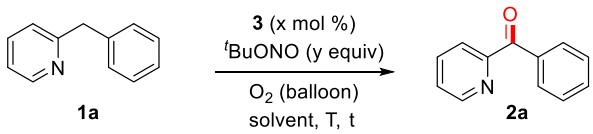
ref. 5: O_2, 10 mol% $CuCl_2$, $ClCH_2CO_2Et$, DMF, 130 °C, 51%
this work: O_2, 5 mol% NHPI, TBN, PhCN, 80 °C, 70%

Recently, we reported that NHPI-^{t}BuONO (TBN) system could mediate the benzyl ammoxidation under transition metal-free conditions,[10] in which the regeneration of PINO radical from NHPI is promoted by TBN under O_2. Herein we report our latest results in the development of NHPI catalyzed heterobenzylic oxygenation of alkylpyridines and the related heteroarenes in the presence of O_2 to achieve heterocyclic ketones (Scheme 1b). The transition metal-free conditions avoid the chelation of

pyridine or acylpyridines to metal catalysts. In addition, the large amount of TBN ensures the high efficiency for PINO regeneration, which is necessary for high efficient generation of benzylic radical intermediates. This method provides a practical and convenient access to pharmaceuticals containing substituted aromatic ketones from the environmental and economic viewpoints.

Initially, the reaction conditions were investigated using 2-benzylpyridine **1a** as a model substrate. Stoichiometric NHPI and TBN in the presence of O_2 atmosphere in DMF at 80 °C afforded the desired product **2a** in 39% yield (Table 1, entry 1). Among the solvents screened, PhCN gave the optimal yield (entries 1-6). To improve the reactivity of the reaction, the amounts of reagent NHPI, TBN, and the reaction time were investigated. It was found that **2a** was obtained in high yield in with 5 mol% NHPI catalyst and 2.0 equiv TBN for 24 h (entries 6−8, and 10−11). NHPI is better than hydroxybenzotriazole (HOBt) or 1-Hydroxy-7-azabenzotriazole (HOAt) (entries 12-14). The necessity of both NHPI and TBN is also confirmed by control experiments (entries 15-17).

Table 1. Screening of Reaction Conditions[a]



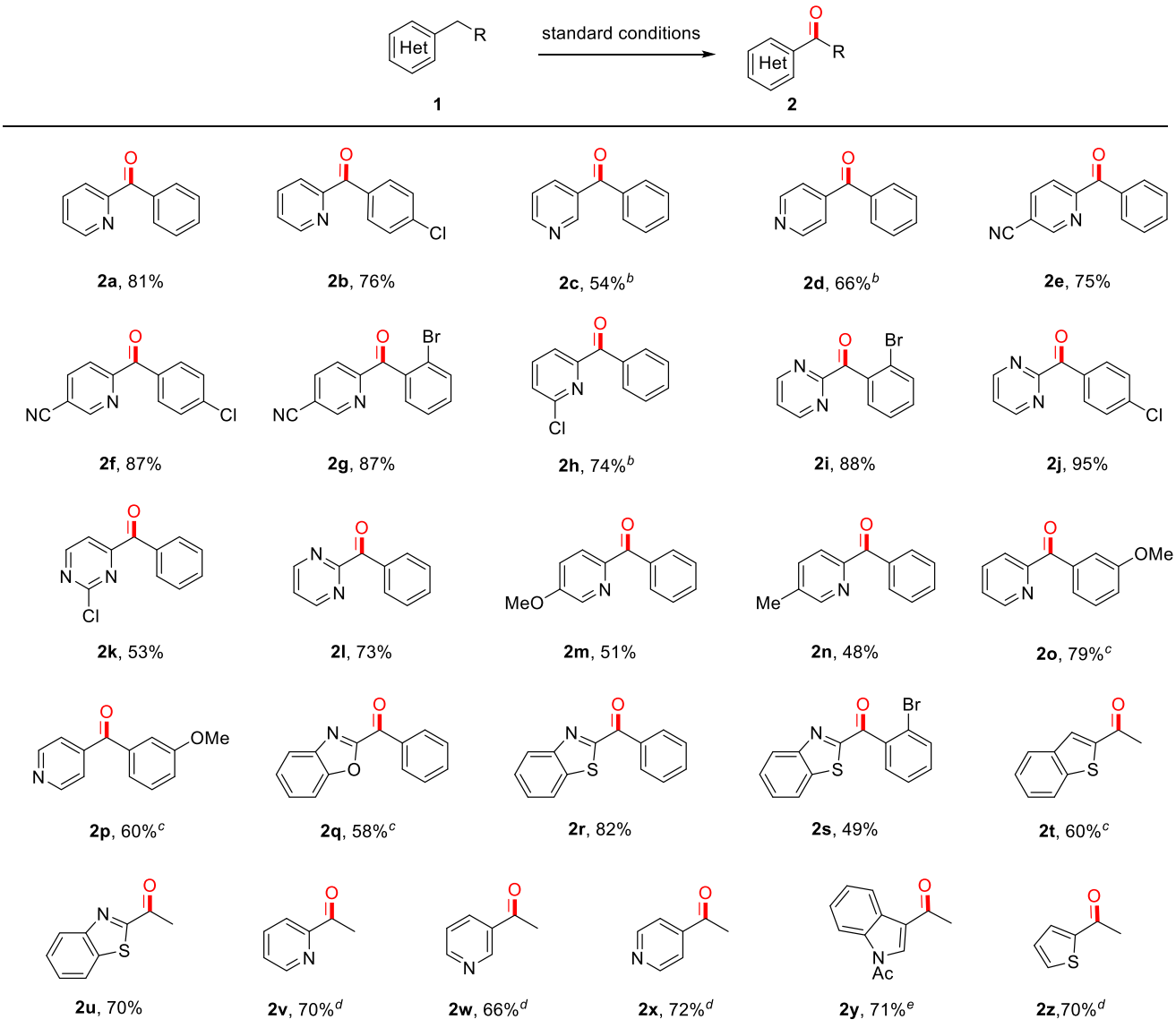
1a **2a**

entry	**3**	*x*	*y*	solvent	temperature(°C)	t(h)	**2a**(%)[b]
1	NHPI	100	2.0	DMF	80	12	39
2	NHPI	100	2.0	$(CF_3)_2CHOH$	80	12	86
3	NHPI	100	2.0	THF	80	12	6
4	NHPI	100	2.0	PhCl	80	12	66
5	NHPI	100	2.0	PhCN	80	12	90
6	NHPI	100	2.0	MeCN	80	12	80
7	NHPI	10	2.0	PhCN	80	12	85
8	NHPI	10	1.0	PhCN	80	12	82
9	NHPI	10	1.0	PhCN	90	12	72
10	NHPI	10	1.0	PhCN	70	12	60
11	NHPI	5	2.0	PhCN	80	12	56
12	NHPI	5	2.0	PhCN	80	24	89
13	HOBt	5	2.0	PhCN	80	24	43
14	HOAt	5	2.0	PhCN	80	24	54
15	NHPI	5	0	PhCN	80	24	35
16	none	5	2.0	PhCN	80	24	0
17[c]	NHPI	5	2.0	PhCN	80	24	29

[a] Conditions: **1a** (0.5 mmol), solvent (1 mL). [b] ^1H NMR yield was reported using nitromethane and *tert*-butyl methyl ether as internal standard. [c] In the absence of O_2.

Subsequently, the scope of the substrate has been investigated under optimized conditions (Table 1, entry 12). Various hetero-benzylic methylenes bearing different functional groups were subjected to the optimized conditions, and the corresponding ketone products were obtained in moderate to good yields (Scheme 2). A variety of heterobenzylic methylene derivatives bearing electron withdrawing substituents in aryl groups such as cyano-, chloro-, and bromo aryl groups were well oxidized to the corresponding ketones (**2b**, **2e-h**). The substrates with electron donating heterocyclic substituents gave lower yields (**2m-n**), while the substrates with electron donating aryl substituents gave moderate to good yields (**2o-p**). Other alkyl on the *N*-containing five-membered heterocycles were evaluated and the corresponding ketones were achieved in 49-82% yields (**2q-2u**). 2-Ethylpyridine **1v** is less reactive substrate under standard conditions, because the electron deficient heterocycles is not favorable for the stabilization of the benzylic radical intermediates. Increasing the loading of NHPI results in improved yields of **2v**. Oxidations of **1w-z** under similar conditions afforded **2w-z** in good yields too.

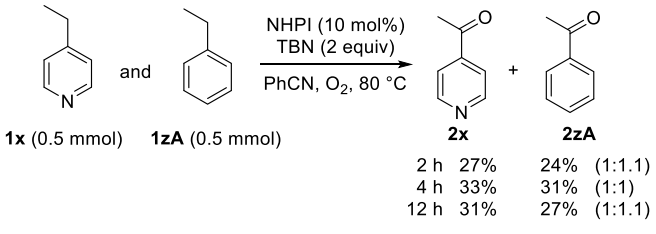
Scheme 2. Scope of Aryl Heterocyclic Benzylic Oxidation[a]



[a] Standard conditions: 1 (0.5 mmol), NHPI (5 mol %.), TBN (2 equiv), PhCN (0.5 M), 80 °C, O_2, 24 h, isolated yield. [b] NHPI (10 mol%). [c] NHPI (15 mol %). [d] NHPI (50 mol %), MeCN (0.5 M). [e] NHPI (50 mol %), TBN (1.0 equiv), MeCN (0.5 M).

A comparison of reactivity of **1x** and **1zA** shows that this metal-free method has no obvious negative effect for heterocycles (Scheme 3).

Scheme 3. Competitive Reaction between Aryl Heterocyclic Benzylic oxidation and Aryl Benzylic Oxidation



In conclusion, we have developed a metal-free organocatalyzed aerobic heterobenzylic C-H oxidation for the synthesis of acylpyri-dines and related derivatives from corresponding alkyl- or aryl heteroarenes. This reaction provides a powerful method for overcoming the electron-withdrawing effect as well as product-inhibition effects in heterobenzylic radical oxidation. A variety of *N*-heterocyclic ketones could be prepared under relatively mild conditions.

EXPERIMENTAL SECTION

General information. All reactions were carried out under atmospheric pressure. Solvents were pre-dried over activated 4 Å molecular sieves and heated to reflux over calcium hydride (PhCN, CH_3CN, DCM, Et_3N, THF, DMF, DCE, PhCl, HFIP, DMSO) under argon atmosphere and collected by distillation. ^1H, ^{13}C NMR spectra were recorded on a Bruker 400 spectrometer; Chemical shifts are reported in δ units relative to $CDCl_3$ [^1H δ = 7.26, ^{13}C δ = 77.16]. HRMS were recorded by the mass spectrometry service at University of Science and Technology

of China (Cl-35, Br-79). Methylarenes and other chemicals without notes in experimental section were purchased from commercial sources.

Procedure for the Synthesis of Starting Compounds 1. Compounds **1f**, **1g**, **1j**, **1k**, **1m**, and **1s** were synthesized by reported procedure.[2a]

6-(4-Chlorobenzyl)nicotinonitrile **(1f)**. Obtained as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.86 (dt, *J* = 8.1 Hz, 1.7 Hz, 1H), 7.29 (dd, *J* = 8.2 Hz, 1.1 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 2H), 4.18 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.8, 152.2, 139.7, 136.3, 132.8, 130.5, 129.0, 123.0, 116.8, 107.7, 44.1. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{10}ClN_2$ 229.0527, found 229.0532. Melting point: 62-64 °C.

6-(2-Bromobenzyl)nicotinonitrile **(1g)**. Obtained as a light orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 1.9 Hz, 1H), 7.83 (dd, *J* = 8.1 Hz, 2.2 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 4.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.11-7.17 (m, 1H), 4.36 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.0, 152.2, 139.6, 137.3, 133.1, 131.8, 128.9, 127.9, 124.9, 123.1, 116.8, 107.6, 44.8. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{10}BrN_2$ 273.0022, found 273.0023.

(2-(4-Chlorobenzyl)pyrimidine) **(1j)**. Obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.9 Hz, 2H), 7.25-7.31 (m, 4H), 7.13 (t, *J* = 4.9 Hz, 1H), 4.26 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.5, 157.3, 136.6, 132.4, 130.5, 128.6, 118.7, 45.2. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{11}H_{10}ClN_2$ 205.0527, found 205.0529.

4-Benzyl-2-chloropyrimidine **(1k)**. Obtained as a deep orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 5.1 Hz, 1H), 7.33-7.37 (m, 2H), 7.25-7.31 (m, 3H), 7.00 (d, *J* = 5.1 Hz, 1H), 4.11 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.3, 161.3, 159.5, 136.5, 129.4, 129.1, 127.4, 118.9, 44.0. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{11}H_{10}ClN_2$ 205.0527, found 205.0527. Melting point: 56-57 °C.

2-Benzyl-5-methoxypyridine **(1m)**. Obtained as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 2.9 Hz, 1H), 7.24-7.32 (m, 4H), 7.21 (t, *J* = 7.0 Hz, 1H), 7.07-7.12 (m, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 4.11 (s, 2H), 3.80 (d, *J* = 11.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.0, 153.1, 140.1, 136.6, 129.0, 128.6, 126.3, 123.2, 121.4, 55.6, 43.7. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{14}NO$ 200.1070, found 200.1071. Melting point: 62-64 °C.

2-(2-Bromobenzyl)benzo[d]thiazole **(1s)**. Obtained as a light yellow solid. ^{1}H NMR (400 MHz, CDCl3) δ 8.01 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.43-7.47 (m, 1H), 7.40-7.42 (m, 1H), 7.28-7.36 (m, 2H), 7.17 (td, *J* = 7.8 Hz, 1.7 Hz, 1H), 4.60 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.8, 153.3, 137.0, 135.7, 133.3, 131.5, 129.3, 128.0, 126.1, 125.0, 124.9, 122.9, 121.6, 40.8. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}BrNS$ 303.9790, found 303.9792. Melting point: 68-69 °C.

General Procedure for Aerobic heterobenzylic C-H oxidation. *N*-hydroxyphthalimide **3** (0.05-0.5 equiv) was weighted into a Schlenk tube. After dried in vacuum for 15 min, dry PhCN (1 mL) was added under an oxygen atmosphere followed by the addition of ^{t}BuONO (1.0-2.0 equiv). **1** (0.5 mmol) was then added and the reaction mixture was stirred at 80 °C by oil bath and monitored by TLC analysis until the complete consumption of **1**. Next, the reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (2 mL), concentrated and purified by column chromatography to give the pure product **2**.

Gram-Scale Preparation of 2g. *N*-hydroxyphthalimide **3** (0.5 mmol, 0.05 equiv, 81.5 mg) was weighted into a Schlenk tube. After dried in vacuum for 15 min, dry PhCN (20 mL) was added under an oxygen atmosphere followed by the addition of ^{t}BuONO (20 mmol, 2.0 equiv, 2.4 mL). **1g** (10 mmol, 1.0 equiv, 2.73g) was then added and the reaction mixture was stirred at 80 °C by oil bath for 24h. Next, the reaction mixture was cooled to room temperature and purified by column chromatography (PE/EA =10:1) to give the pure product **2g**, light yellow solid (2.44g, 85% yield).

Phenyl(pyridin-2-yl)methanone **(2a).**[6] **2a** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =10:1), light yellow oil (74.2 mg, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.00-8.06 (m, 3H), 7.83-7.90 (m, 1H), 7.54-7.59 (m, 1H), 7.43-7.49 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.9, 155.1, 148.6, 137.1, 136.3, 132.9, 131.0, 128.2, 126.2, 124.6.

(4-Chlorophenyl)(pyridin-2-yl)methanone **(2b).**[5] **2b** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =20:1), light white solid (82.7 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 3.3 Hz, 1H), 8.07 (d, *J* = 7.4 Hz, 3H), 7.92 (t, *J* = 7.4 Hz, 1H), 7.45-7.52 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.5, 154.7, 148.6, 139.5, 137.3, 134.6, 132.6, 128.6, 126.5, 124.8.

Phenyl(pyridin-3-yl)methanone **(2c).** [6] **2c** was prepared according to the general procedure using NHPI (0.05 mmol, 0.1 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =3:1), light yellow oil (49.4 mg, 54% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.82 (s, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.82 (d, *J* = 7.4 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.46 (q, *J* = 4.9 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.0, 153.0, 151.1, 137.3, 136.8, 133.3, 130.2, 128.8, 123.5.

Phenyl(pyridin-4-yl)methanone **(2d).**[6] **2c** was prepared according to the general procedure using NHPI (0.05 mmol, 0.1 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =3:1), light yellow oil (60.4 mg, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 5.9 Hz, 2H), 7.81 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.58 (d, *J* = 5.9 Hz, 2H), 7.51 (t, *J* = 7.9 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.1, 150.3, 144.4, 135.9, 133.6, 130.2, 128.7, 123.0.

6-Benzoylnicotinonitrile **(2e)** [2a] **2e** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =10:1), light yellow solid (78.1 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (t, *J* = 1.9 Hz, 0.9 Hz, 1H), 8.13-8.20 (m, 2H), 8.04-8.06 (m, 2H), 7.62-7.66 (m, 1H), 7.51 (t, *J* = 7.9 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.1, 157.4, 151.2, 140.6, 135.2, 133.8, 131.1, 128.5, 124.4, 116.1, 112.1. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_9N_2O$ 209.0709, found 209.0708. Melting point: 92-93 °C.

6-(4-Chlorobenzoyl)nicotinonitrile **(2f). 2f** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash

column chromatography (PE/EA =10:1), light yellow solid (105.6 mg, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.16-8.22 (m, 2H), 8.06 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.6, 157.0, 151.2, 140.8, 140.5, 133.6, 132.6, 128.9, 124.5, 116.1, 112.4. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_8ClN_2O$ 243.0320, found 243.0327. Melting point: 125-127 °C.

6-(2-Bromobenzoyl)nicotinonitrile **(2g). 2g** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =10:1), light yellow solid (125.2 mg, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.22 (qd, *J* = 8.1 Hz, 0.8 Hz, 2H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.44-7.48 (m, 2H), 7.38-7.43 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.5, 155.6, 151.9, 140.8, 139.2, 133.2, 132.4, 130.2, 127.5, 123.4, 120.3, 116.1, 112.8. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_8BrN_2O$ 286.9815, found 286.9820. Melting point: 125-128 °C.

(6-Chloropyridin-2-yl)(phenyl)methanone **(2h).**[2a] **2c** was prepared according to the general procedure using NHPI (0.05 mmol, 0.1 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =50:1), light yellow oil (80.1 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.10 (m, 2H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.86 (t, *J* = 7.8 Hz, 1H), 7.59-7.63 (m, 1H), 7.47-7.54 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.0, 155.4, 150.4, 139.8, 135.6, 133.4, 131.2, 128.4, 127.2, 123.3.

(2-Bromophenyl)(pyrimidin-2-yl)methanone **(2i).**[11] **2i** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =3:1), light yellow solid (116.0 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 4.9 Hz, 2H), 7.60-7.62 (m, 2H), 7.46 (q, *J* = 12.0 Hz, 2H), 7.39 (dt, *J* = 7.4 Hz, 1.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.6, 161.2, 157.8, 139.6, 133.2, 132.6, 130.8, 127.6, 122.7, 120.7.

(4-Chlorophenyl)(pyrimidin-2-yl)methanone **(2j).**[2a] **2j** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =3:1), light yellow solid (104.4 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (d, *J* = 4.9 Hz, 2H), 8.02 (d, *J* = 8.5 Hz, 2H), 7.50 (t, *J* = 4.9 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.0, 162.2, 157.5, 140.3, 133.5, 132.4, 128.8, 122.5. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{11}H_8ClN_2O$ 219.0320, found 219.0320. Melting point: 90-92 °C.

(2-Chloropyrimidin-4-yl)(phenyl)methanone **(2k). 2k** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =10:1), light yellow oil (58.0 mg, 53% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 4.9 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 2H), 7.81 (d, *J* = 5.0 Hz, 1H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.1 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.5, 164.3, 161.5, 161.0, 134.4, 134.3, 131.1, 128.7, 118.9. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{11}H_8ClN_2O$ 219.0320, found 219.0319.

Phenyl(pyrimidin-2-yl)methanone **(2l). 2l** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =3:1), light yellow oil (67.2 mg, 73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J* = 4.9 Hz, 2H), 7.99 (dd, *J* = 8.2 Hz, 1.0 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.43-7.47 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.3, 162.6, 157.4, 135.0, 133.7, 130.9, 128.4, 122.3. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{11}H_9N_2O$ 185.0709, found 185.0710.

(5-Methoxypyridin-2-yl)(phenyl)methanone **(2m).**[2a] **2m** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =5:1), light orange oil (54.7 mg, 51% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 2.9 Hz, 1H), 8.10 (d, *J* = 8.7 Hz, 1H), 8.04 (d, *J* = 7.0 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.32 (dd, *J* = 7.8 Hz, 1.9 Hz, 1H), 3.93 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.0, 157.8, 147.6, 137.0, 136.7, 132.5, 130.9, 128.1, 126.4, 120.2, 55.9.

(5-Methylpyridin-2-yl)(phenyl)methanone **(2n).**[2a] **2n** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =10:1), light yellow oil (47.5 mg, 48% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.05 (d, *J* = 7.1 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.0, 152.7, 149.2, 137.5, 136.7, 136.7, 132.9, 131.1, 128.2, 124.5, 18.8.

(3-Methoxyphenyl)(pyridin-2-yl)methanone **(2o)**[12] **2o** was prepared according to the general procedure using NHPI (0.075 mmol, 0.15 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =5:1), brown liquid (84.1 mg, 79% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71-8.72 (m, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.89 (t, *J* = 7.7 Hz, 1H), 7.60-7.62 (m, 2H), 7.46-7.49 (m, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.12-7.15 (m, 1H), 3.85 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.8, 159.5, 155.2, 148.7, 137.6, 137.1, 129.3, 126.3, 124.7, 124.0, 119.6, 115.2, 55.5.

(3-Methoxyphenyl)(pyridin-4-yl)methanone **(2p)**[13] **2p** was prepared according to the general procedure using NHPI (0.075 mmol, 0.15 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =5:1), white solid (63.8 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80-8.81 (m, 2H), 7.58-7.59 (m, 2H), 7.32-7.43 (m, 3H), 7.17-7.20 (m, 1H), 3.87 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.0, 159.9, 150.4, 144.5, 137.2, 129.7, 123.1, 122.9, 120.1, 114.2, 55.6.

Benzo[d]oxazol-2-yl(phenyl)methanone **(2q)**[3b] **2q** was prepared according to the general procedure using NHPI (0.075 mmol, 0.15 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =20:1), light yellow solid (65.2 mg, 58% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54-8.56 (m, 2H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.70 (q, *J* = 8.2 Hz, 2H), 7.54-7.59 (m, 3H), 7.48 (t, *J* = 8.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 180.7, 157.2, 150.5, 140.9, 135.1, 134.4, 131.1, 128.8, 128.6, 125.7, 122.5, 112.0.

Benzo[d]thiazol-2-yl(phenyl)methanone **(2r).**[3b] **2r** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =20:1), light yellow solid (98.5 mg, 82% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 8.4 Hz, 2H), 8.24 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.65-7.69 (m, 1H), 7.54-7.58 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.4, 167.2, 153.9, 137.1, 135.0, 134.0, 131.4, 128.6, 127.7, 127.0, 125.8, 122.3.

Benzo[d]thiazol-2-yl(2-bromophenyl)methanone **(2s). 2s** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =20:1), light yellow solid (77.9 mg, 49% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-8.18 (m, 1H), 8.01-8.03 (m, 1H), 7.70-7.74 (m, 2H), 7.54-7.59 (m, 2H), 7.48 (td, *J* = 7.5 Hz, 1.1 Hz, 1H), 7.43 (td, *J* = 7.7 Hz, 1.8 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 188.4, 165.8, 153.8, 138.1, 137.6, 133.8, 132.5, 130.8, 128.1, 127.2, 127.2, 126.1, 122.5, 120.7. HRMS (ESI−TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_9BrNOS$ 317.9583, found 317.9586. Melting point: 103-105 °C.

1-(Benzo[b]thiophen-2-yl)ethan-1-one **(2t).**[14] **2t** was prepared according to the general procedure using NHPI (0.075 mmol, 0.15 equiv), TBN (0.5 mmol, 1.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =20:1), light yellow solid (52.5 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.88 (t, *J* = 8.5 Hz, 2H), 7.45-7.49 (m, 1H), 7.39-7.43 (m, 1H), 2.67 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.4, 144.1, 142.7, 139.2, 129.8, 127.6, 126.0, 125.1, 123.1, 26.9.

1-(Benzo[d]thiazol-2-yl)ethan-1-one **(2u)**[5] **2u** was prepared according to the general procedure using NHPI (0.025 mmol, 0.05 equiv), TBN (1.0 mmol, 2.0 equiv), 24 h, and purified by flash column chromatography (PE/EA =20:1), light yellow solid (61.8 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (ddd, *J* = 8.2 Hz, 1.2 Hz, 0.9 Hz, 1H), 7.98 (ddd, *J* = 8.4 Hz, 1.3 Hz, 0.6 Hz, 1H), 7.51-7.60 (m, 2H), 2.83 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.3, 166.6, 153.7, 137.5, 127.8, 127.1, 125.6, 122.6, 26.3.

1-(Pyridin-2-yl)ethan-1-one **(2v).**[5] **2v** was prepared according to the general procedure using NHPI (0.25 mmol, 0.5 equiv), TBN (1.0 mmol, 2.0 equiv), MeCN (1 mL), 24 h, and purified by flash column chromatography (PE/EA =10:1), light yellow oil (42.4 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.94-7.98 (m, 1H), 7.75-7.78 (m, 1H), 7.39-7.42 (m, 1H), 2.64-2.66 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.1, 153.5, 149.0, 136.8, 127.1, 121.6, 25.8.

1-(Pyridin-3-yl)ethan-1-one **(2w)** [5] **2w** was prepared according to the general procedure using NHPI (0.25 mmol, 0.5 equiv), TBN (1.0 mmol, 2.0 equiv), MeCN (1 mL), 24 h, and purified by flash column chromatography (PE/EA =10:1), light yellow oil (40.0 mg, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.66-8.68 (m, 1H), 8.11-8.13 (m, 1H), 7.26-7.33 (m, 1H), 2.55 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.7, 153.5, 149.8, 135.4, 132.1, 123.6, 26.6.

1-(Pyridin-4-yl)ethan-1-one **(2x).**[5] **2x** was prepared according to the general procedure using NHPI (0.25 mmol, 0.5 equiv), TBN (1.0 mmol, 2.0 equiv), MeCN (1 mL), 24 h, and purified by flash column chromatography (PE/EA =10:1), light yellow oil (44.0 mg, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 5.4 Hz, 2H), 7.68 (d, *J* = 5.8 Hz, 2H), 2.58 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.4, 151.0, 142.7, 121.2, 26.7.

1,1'-(1H-indole-1,3-diyl)bis(ethan-1-one) **(2y)** [15] 2**y** was prepared according to the general procedure using NHPI (0.25 mmol, 0.5 equiv), TBN (0.5 mmol, 1.0 equiv), MeCN (1 mL), 24 h, and purified by flash column chromatography (PE/EA =5:1), light yellow oil (71.5 mg, 71% yield). ^{1}H NMR (CDCl3, 400 MHz): δ 8.33-8.36 (m, 2H), 7.99-8.03 (m, 1H), 7.39-7.40 (m, 2H), 2.70 (s, 3H), 2.56 (s, 3H). ^{13}C{^{1}H} NMR (CDCl3, 100 MHz): δ 193.8, 168.8, 136.1, 131.3, 127.3, 126.4, 125.3, 122.6, 122.0, 116.2, 28.0, 24.2.

1-(Thiophen-2-yl)ethan-1-one **(2z).**[16] **2z** was prepared according to the general procedure using NHPI (0.25 mmol, 0.5 equiv), TBN (1.0 mmol, 2.0 equiv), MeCN (1 mL), 24 h, and purified by flash column chromatography (PE/EA =20:1), light yellow oil (44.2 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 3.8 Hz, 1.1 Hz, 1H), 7.61 (dd, *J* = 5.0 Hz, 1.1 Hz, 1H), 7.10 (dd, *J* = 5.0 Hz, 3.8 Hz, 1H), 2.53 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 190.8, 144.6, 133.9, 132.6, 128.2, 26.9.

ASSOCIATED CONTENT

Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.
NMR spectra (PDF).

AUTHOR INFORMATION

Corresponding Author

* E-mail: ybkang@ustc.edu.cn
* E-mail: ias_jpqu@njtech.edu.cn

ORCID

Jian-Ping Qu: 0000-0002-5002-5594
Yan-Biao Kang: 0000-0002-7537-4627

Notes

Any additional relevant notes should be placed here.

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REFERENCES

1 a) Li, X.; Jiao, N. Reoxidation of Transition-metal Catalysts with O_2. *Chin. J. Chem.* **2017**, *35*, 1349-1365; b) Liang, Y.-F.; Jiao, N. Oxygenation via C–H/C–C Bond Activation with Molecular Oxygen. *Acc. Chem. Res.* **2017**, *50*, 1640-1653; c) Bian, C.; Singh, A. K.; Niu, L.; Yi, H.; Lei, A. Visible-Light-Mediated Oxygenation Reactions using Molecular Oxygen. *Asian J. Org. Chem.* **2017**, *6*, 386-396; d) Campbell, A. N.; Stahl, S. S. Overcoming the "Oxidant Problem": Strategies to Use O_2 as the Oxidant in Organometallic C–H Oxidation Reactions Catalyzed by Pd (and Cu). *Acc. Chem. Res.* **2012**, *45*, 851-863; e) Shi, Z.; Zhang, C.; Tang, C.; Jiao, N. Recent advances in transition-metal catalyzed reactions using molecular oxygen as the oxidant. *Chem. Soc. Rev.* **2012**, *41*, 3381-3430; f) Liu, C.; Zhang, H.; Shi, W.; Lei, A. Bond Formations between Two Nucleophiles: Transition Metal Catalyzed Oxidative Cross-Coupling Reactions. *Chem. Rev.* **2011**, *111*, 1780-1824; g) Ishii, Y.; Sakaguchi, S.; Obora, Y. Aerobic Oxidations and Related Reactions Catalyzed by N-Hydroxyphthalimide, in Modern Oxidation Methods, 2nd Ed. (Ed Bäckval, J. E.), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 2010. pp187-240; h) Ishii, Y.; Sakaguchi, S.; Iwahama, T. Innovation of Hydrocarbon Oxidation with Molecular Oxygen and Related Reactions. *Adv. Synth. Catal.* **2001**, *343*, 393-427.

2 For selected examples on aerobic benzylic oxidative synthesis of ketones from alkyl arenes: a) Sterckx, H.; De

Houwer, J.; Mensch, C.; Herrebout, W.; Tehrani, K. A.; Maes, B. U. W. Base metal-catalyzed benzylic oxidation of (aryl)(heteroaryl)methanes with molecular oxygen. *Beilstein J. Org. Chem*. **2016**, *12*, 144-153; b) Shen, D.; Miao, C.; Wang, S.; Xia, C.; Sun, W. Efficient Benzylic and Aliphatic C–H Oxidation with Selectivity for Methylenic Sites Catalyzed by a Bioinspired Manganese Complex. *Org. Lett.* **2014**, *16*, 1108-1111; c) Ishii, Y.; Nakayama, K.; Takeno, M.; Sakaguchi, S.; Iwahama, T.; Nishiyama, Y. Novel Catalysis by N-Hydroxyphthalimide in the Oxidation of Organic Substrates by Molecular Oxygen. *J. Org. Chem.* **1995**, *60*, 3934-3935.

3 a) Houwer, J. D.; Tehrani, A. K.; Maes, B. U. W. Synthesis of Aryl(di)azinyl Ketones through Copper- and Iron-catalyzed Oxidation of the Methylene Group of Aryl(di)azinylmethanes. *Angew. Chem. Int. Ed.* **2012**, *51*, 2745-2748; b) Sterckx, H.; De Houwer, J.; Mensch, C.; Caretti, I.; Tehrani, K. A.; Herrebout, W. A.; Van Doorslaer, S.; Maes, B. U. W. Mechanism of the Cu^{II}-catalyzed benzylic oxygenation of (aryl)(heteroaryl)methanes with oxygen. *Chem. Sci*. **2016**, *7*, 346-357.

4 Ren, L.; Wang, L.; Lv, Y.; Li, G.; Gao, S. Synergistic H_4NI-AcOH Catalyzed Oxidation of the $C_{sp}{}^3$-H Bonds of Benzylpyridines with Molecular Oxygen. *Org. Lett.* **2015**, *17*, 2078-2081.

5 Liu, J.; Zhang, X.; Yi, H.; Liu, C.; Liu, R.; Zhang, H.; Zhuo, K.; Lei, A. Chloroacetate-Promoted Selective Oxidation of Heterobenzylic Methylenes under Copper Catalysis. *Angew. Chem. Int. Ed.* **2015**, *54*, 1261-1265.

6 Hruszkewycz, D. P.; Miles, K. C.; Thiel, O. R.; Stahl, S. S. Co/NHPI-mediated aerobic oxygenation of benzylic C–H bonds in pharmaceutically relevant molecules. *Chem. Sci.* **2017**, *8*, 1282-1287.

7 Masui, M.; Hara, S.; Ueshima, T.; Kawaguchi, T.; Ozaki, S. Anodic Oxidation of Compounds Having Benzylic or Allylic Carbon and α-Carbon to Hetero Atom Using N-Hydroxyphthalimide as A Mediator. *Chem. Pharm. Bull*. **1983**, *31*, 4209-4211.

8 Cooper, J. C.; Luo, C.; Kameyama, R.; Humbeck, J. F. V. Combined Iron/Hydroxytriazole Dual Catalytic System for Site Selective Oxidation Adjacent to Azaheterocycles. *J. Am. Chem. Soc*. **2018**, *140*, 1243-1246.

9 For recent metal-Free examples: a) Jin, W.; Zheng, P.; Wong, W.-T.; Law, G.-L. Efficient Selenium-Catalyzed Selective C(sp^3)–H Oxidation of Benzylpyridines with Molecular Oxygen. *Adv. Synth. Catal.* **2017**, *359*, 1588-1593; b) Yang, F.; Zhou, B.; Chen, P.; Zou, D.; Luo, Q.; Ren, W.; Li, L.; Fan, L.; Li, J. Transition-Metal-Free C(sp^3)–H Oxidation of Diarylmethanes. *Molecules* **2018**, *23*, 1922-1927; c) Wang, H.; Wang, Z.; Huang, H.; Tan, J.; Xu, K. KO^{t}Bu-Promoted Oxidation of (Hetero)benzylic $C_{sp}{}^3$–H to Ketones with Molecular Oxygen. *Org. Lett.* **2016**, *18*, 5680-5683.

10 a) Ning, X.-S.; Wang, M.-M.; Yao, C.-Z.; Chen, X.-M.; Kang, Y.-B. *tert*-Butyl Nitrite: Organic Redox Cocatalyst for Aerobic Aldehyde-Selective Wacker-Tsuji Oxidation. *Org. Lett.* **2016**, *18*, 2700-2703; b) Chen, X.-M.; Ning, X.-S.; Kang, Y.-B. Aerobic Acetoxyhydroxylation of Alkenes Co-catalyzed by Organic Nitrite and Palladium. *Org. Lett.* **2016**, *18*, 5368-5371; c) Wang, M.-M.; Ning, X.-S.; Qu, J.-P.; Kang, Y.-B. Dehydrogenative Synthesis of Linear α,β-Unsaturated Aldehydes with Oxygen at Room Temperature Enabled by ^{t}BuONO. *ACS Catal.* **2017**, *7*, 4000-4003; d) Hu, K.-F.; Ning, X.-S.; Qu, J.-P.; Kang, Y.-B. Tuning Regioselectivity of Wacker Oxidation in One Catalytic System: Small Change Makes Big Step. *J. Org. Chem.* **2018**, *83*, 11327-11332; e) Ning, X.-S.; Wang, M.-M.; Qu, J.-P.; Kang, Y.-B. Synthesis of Functionalized Indoles via Palladium-Catalyzed Aerobic Cycloisomerization of *o*-Allylanilines Using Organic Redox Cocatalyst. *J. Org. Chem.* **2018**, *83*, 13523-13529.

11 Stolle, W.A.W.; Marcelis, A.T.M.; Koetsier, A.; van der Plas, H.C. Intramolecular Diels-Alder reactions of pyrimidines: Synthesis of tricyclic annelated pyridines. *Tetrahedron Lett*. **1989**, *45*, 6511-6518.

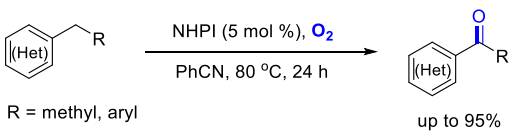
12 Guha, S.; Sekar, G. Metal-Free Halogen(I) Catalysts for the Oxidation of Aryl(heteroaryl)methanes to Ketones or Esters: Selectivity Control by Halogen Bonding. *Chem. Eur. J*. **2018**, *24*, 14171-14182.

13 Bosch, J.; Bonjoch, J.; Diez, A.; Linares, A.; Moral, M.; Rubiralta, M. Mercuric acetate cyclization of 4-(arylmethyl)piperidines; synthesis of indolo [2,3-g]morphans (tetracyclic ring system of strychnos indole alkaloids) and 7,8-benzomorphans. *Tetrahedron* **1985**, *9*, 1753-1762;

14 Tosa, M. I.; Podea, P. V.; Paizs, C.; Irimie, F. D. Chemoenzymatic synthesis of (*R*)- and (*S*)-1-heteroarylethanols. *Tetrahedron: Asymmetry* **2008**, *19*, 2068-2071.

15 Kamijo, S.; Amaoka, Y.; Inoue, M. Unified Oxidation Protocol for the Synthesis of Carbonyl Compounds Using a Manganese Catalyst. *Synthesis*. **2010**, *14*, 2475-2489.

16 Cai, M.; Zheng, G.; Ding, G. The first heterogeneous carbonylative Stille coupling of organostannanes with aryl iodides catalyzed by MCM-41-supported bidentate phosphine palladium(0) complex. *Green Chem*. **2009**, *11*, 1687-1693.



R = methyl, aryl

up to 95%