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Cross Redox Coupling of Aryl-Aldehydes and *p*-Benzoquinone

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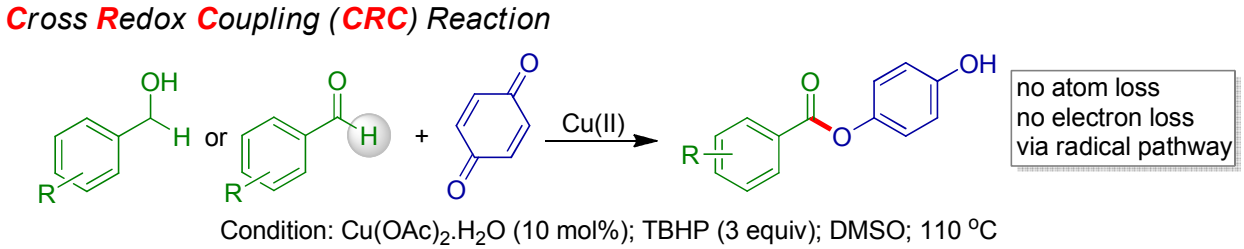
GRAPHIC FOR TOC



ABSTRACT

Herein we report an unprecedented **C**ross **R**edox **C**oupling (CRC) reaction catalyzed by $Cu(OAc)_2.H_2O$. As a proof-of-concept, direct coupling of aromatic aldehydes (or alcohols) and *p*-benzoquinone led to an ester in presence of Cu(II)-TBHP combination. During the coupling process, C-H bond of the aldehydes were converted directly to C-O bond. Mechanistically, we propose that the reaction proceeded *via* a radical pathway. In addition, atom and electron economies were well-conserved during this CRC reaction.

A redox coupling reaction[1] is known in Fischer indolization reaction[2,3] in which C-C single bond is oxidatively created[4] at the expense of reductive cleavage of N-N bond. Overall, indolization reaction could be rationalized as dehydrogenative α-cross coupling of two ketones to a 1,4-diketone.[5] Similarly, various cross condensation reactions between two carbonyl compounds are well documented in literature e.g., cross aldol condensation,[6] Cannizzaro reaction,[7] coupling of ketones and carboxylate enolates,[5] etc. Undesirably, most of these traditional procedures require strong basic condition, higher temperature and produce unwanted side products.

Benzoquinone and its derivatives[8] are prevalent in organic synthesis. Also, they have versatile use in many research fields like molecular electronics,[9] oxidation chemistry,[10] medicinal chemistry,[11,12] radical reactions,[13,14] etc. The most common reactions of quinones are: nucleophilic addition of thiols and amines to derive substituted hydroquinone derivatives *via* Michael addition[15] and metal[16,17] or hypervalent iodine catalyzed[18] C-H activation.[19-24] However, examples on acylation of hydroquinone directly from quinone with acylating agents are very few, if any.[25] In synthesis, mono esterification of hydroquinone is challenging because of unavailability of suitably activated acid or coupling reagents[8] and uncontrollable diesterification reactions.

We report here direct cross coupling reaction for esterification of two carbonyl compounds (*p*-benzoquinone and benzaldehyde derivatives) (Fig. 1). To the best of our knowledge, coupling reaction between two carbonyls *via* a radical pathway is unprecedented (this work). Nevertheless, cross-coupling of α-alkoxymethyl-trifluoroborates with aryl- and heteroaryl bromides has recently been demonstrated using iridium photoredox-catalyst and Ni-catalyst.[26]

Generally, esters are synthesized using pre-activated acid derivatives (e.g., anhydrides, acyl halides, activated esters, etc.) and alcohols in presence of stoichiometric amount of bases by multistep processes.[27-31] Besides, few modified esterification approaches are: oxidative esterification of aldehydes with *β*-dicarbonyl compounds,[32] C-O coupling by direct C-H bond activation of formamides for synthesis of enol carbamates,[33] Pd-catalyzed oxidative cross-esterifications,[34] *N*-heterocyclic carbene (NHC)[35] catalyzed esterifications of *p*-napthaquinones using aldehydes *via* Breslow intermediate (Fig. 1d),[36] etc.

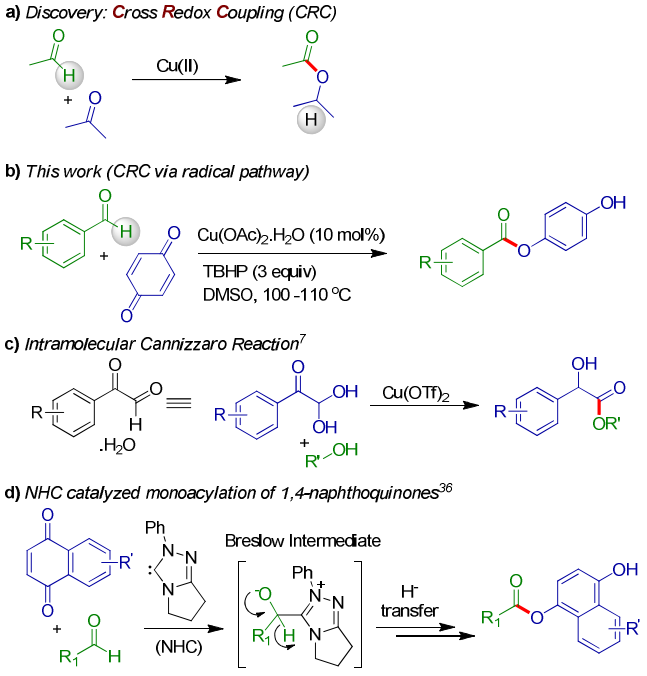


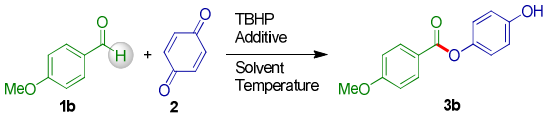
Figure 1. Cross Redox Coupling (CRC) reaction; newly formed C-O bonds are shown as red-thick line and references as superscript. a) Understanding of CRC reaction. b) This work: $Cu(OAc)_2.H_2O$ catalyzed CRC reaction. c) Intramolecular Cannizzaro reaction.[7] d) NHC catalyzed monoacylation of 1,4-napthaquinopne using aldehyde *via* Breslow intermediate.[36]

Table 1 represents optimization of the reaction condition. Most suitable condition (entry 5) was identified using 1.0 equiv of **1b** (*p*-anisaldehyde), 1.5 equiv of **2** (*p*-benzoquinone), 3.0 equiv of TBHP (*Caution!!*, see Caution paragraph in Experimental Section on page 13) and 10 mol% of $Cu(OAc)_2.H_2O$ in DMSO at 100-110 °C. At high temperature (ca. 110 °C) TBHP is known to undergo decomposition. Therefore, excess TBHP (3 equiv, 70% aqueous solution) was required for the reaction. The reaction led to poor yields when temperature was <100 °C and failed in presence of additives like I_2 (entry 8) or KI-I_2 (entry 9). Sluggish mixture was obtained in presence of $CuCl_2$ (entry 11), $Cu(OTf)_2$ (entry 13), $FeCl_3$ (entry 12), etc. Addition of $K_2S_2O_8$ (entry 10) to $Cu(OAc)_2.H_2O$ did not lead to any improvement of yield. Reaction was also unsuccessful with solvents like acetonitrile (entry 1) and dimethyl formamide (entry 2). Conversely, it was poor yielding (ca. 38%) under neat condition (entry 14) and failure under solvent free ball-milling condition[37]

Under optimized condition (Table 1, entry 5), we verified substrates scope for benzoylation of *p*-benzoquinone (Fig. 2). Benzaldehyde and its derivative with electron donating substituents resulted in good yield of the products (**3a**, **3b**, **3c**, **3j**, **3k** and **3l**). Halogen substituted monoesters were also isolated in reasonably fair yields (**3e** and **3f**). Similarly, esters were obtained in good yields with ortho-substituted benzaldehydes (**3d**, **3g**, **3j** and **3m**), hetero-aromatic aldehyde (**3o**) and polynuclear aromatic aldehydes (**3p**, **3q** and **3r**). In presence of TBHP, over-oxidation of benzylic C-H was not observed for the substrate **3c**, **3d**, **3g**, **3h**, **3m** and **3n**. One of the major drawbacks of this CRC reaction in which aldehydes with electron withdrawing group like *p*-nitro and *p*-cyano failed to produce any esters. Also, under similar reaction condition (Table 1, entry 5)

naphthoquinone and 2,6-dimethyl benzoquinone led to unidentifiable mixture of products with benzaldehyde.

Table 1. Optimization of reaction condition for synthesis of **3b**.



Entry	TBHP[a] (equiv)	Additive[b] (mol%)	Solvent[c] (temp, °C)	Yield[d] (%)
1	2	$Cu(OAc)_2.H_2O$	CH_3CN (90 °C)	< 5
2	2	$Cu(OAc)_2.H_2O$	DMF (90 °C)	< 5
3	2	$Cu(OAc)_2.H_2O$	DMSO (90 °C)	36
4	3	$Cu(OAc)_2.H_2O$	DMSO	62
5	3	$Cu(OAc)_2.H_2O$ (10)	DMSO	82
6	3	$Cu(OAc)_2.H_2O$ (5)	DMSO	48
7	3	TBAI (20)	DMSO	30

8	3	I_2 (20)	DMSO	-- [e]
9	3	KI (50) + I_2 (20)	DMSO	-- [e]
10	2	$Cu(OAc)_2.H_2O$ (10) + $K_2S_2O_8$ (20)	DMSO	50
11	3	$CuCl_2$ (20)	DMSO	-- [f]
12	3	$FeCl_3$ (30)	DMSO	< 5
13	3	$Cu(OTf)_2$ (20)	DMSO	-- [e]
14	3	$Cu(OAc)_2.H_2O$	Neat	38 [d]
15	3[g]	$Cu(OAc)_2.H_2O$	DMSO	--[h]
16	3	CuI (20)	DMSO	--[h]
17	3	CuBr (20)	DMSO	--[h]

[a] 70% In water. [b] $Cu(OAc)_2.H_2O$ used in 20 mol% unless specified. [c] In DMSO, the reactions were done at 110 °C, if not shown. [d] Yield based on recovered aldehydes. [e] Not conclusive. [f] Sluggish reaction mixture. [g] 5-6 M TBHP in decane. [h] No reaction.

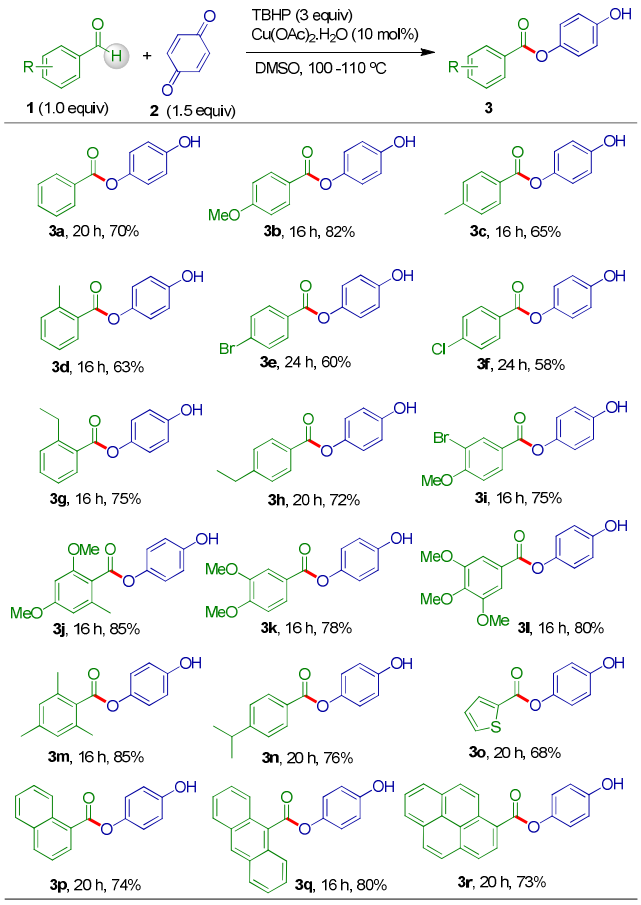


Figure 2. Products from CRC reaction. Compounds identification number, reaction time and yields are shown. Yields (after column chromatography) were calculated based on recovered aldehydes.

We have further extended the scope for this CRC methodology to verify multistep synthesis.[38] Under optimized condition (Fig. 2), primary alcohols were directly used in presence of 4 equiv of TBHP. Expectedly, alcohols were *in situ* oxidized in presence of additional one equivalent of TBHP. The results of this multistep synthesis are shown in Fig. 3.

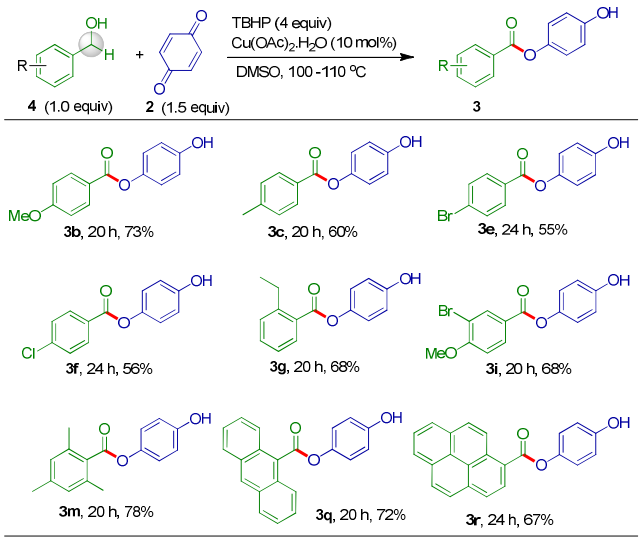


Figure 3. *In situ* oxidation of alcohols to aldehydes for cross redox coupling with *p*-benzoquinones under standard condition. Yields are based on recovered aldehydes.

Control experiments (Fig. 4) in DMSO at 100-110 °C were performed to understand the mechanism of CRC reaction (Fig. 5). 2,2,6,6-Tetramethylpiperidin-1-yl-oxy radical (TEMPO) adduct (**5**, 78%) of *p*-anisaldehyde (**1b**) was observed when the reaction was performed in presence of 2 equiv of TEMPO (Fig. 4a). In absence of either both or any one of the reagents like TBHP and $Cu(OAc)_2.H_2O$, no reaction between *p*-benzoquinone and benzaldehydes were observed (Fig. 4b). Formation of **5** indicates that benzoyl radical might be involved as one of the intermediates (**8**, Fig. 5).

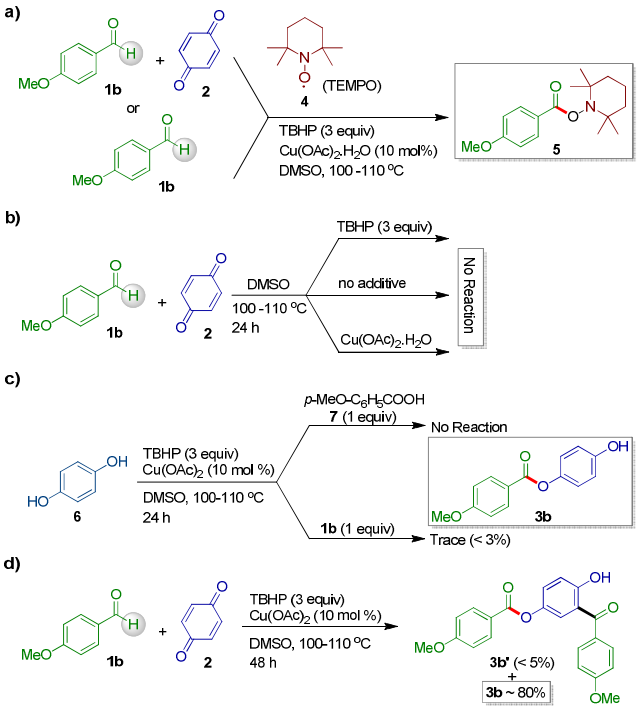


Figure 4. a) - d) Control experiments to understand the mechanism of the reaction.

Furthermore, we could rule out the possibility of complete reduction of *p*-benzoquinone to hydroquinone (**6**) due to inaccessibility of any diester of hydroquinone during reaction. Trace (< 3%) amount of **3b** was detected (Fig. 4c) in between reaction of **1b** and **6**. Likewise, no **3b** could be isolated from reaction of **6** and *p*-anisic acid (**7**). These facts clearly establish that neither hydroquinone nor benzoic acid derivatives (anisic acid) was the intermediate in this reaction. However, when the reaction was continued for more than 48 h, we observed **3b'** as a minor product (< 5%) (Fig. 4d). Interestingly, no direct C-aroylated product before O-aroylation was observed.

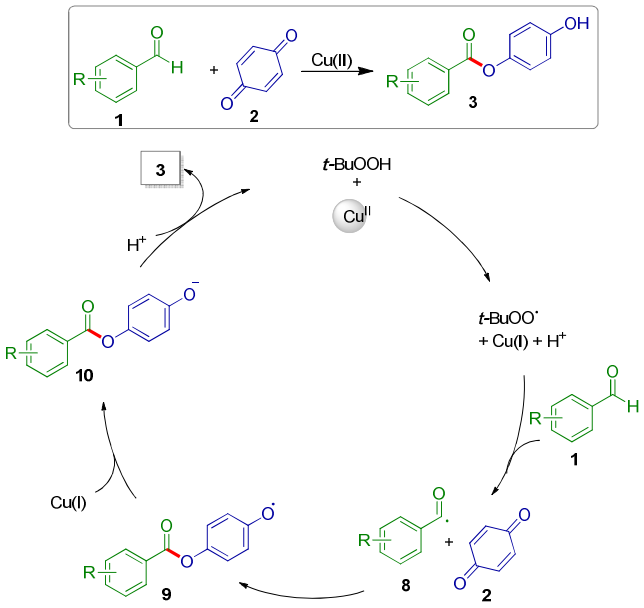


Figure 5. Plausible mechanism for Cu(II) catalyzed CRC reaction.

Plausible mechanism of Cu(II) catalyzed CRC reaction is proposed (Fig. 5) based on the outcome of control experiments (Fig. 4). In presence of Cu(II), *t*-butylperoxy radical (*t*-BuOO$^{\bullet}$) was produced from TBHP. After which *t*-BuOO$^{\bullet}$ could led to aroyl radical (**8**)[39] derived from benzaldehydes (**1**) with release of Cu(I).[40,41] The hydrogen radical (H$^{\bullet}$) produced from TBHP might reduce Cu(II) to Cu(I) to generate H^+. Further, this aroyl radical possibly combined with *p*-benzoquinone *via* O-addition[42] to result in 4-(aroyloxy)phenoxide radical (**9**). Following, Cu(I) expected to reduce **9** into 4-(aroyloxy)phenolate anion (**10**). Finally, **10** yielded the ester **3** in presence of H_3O^+ (TBHP used as 70% in water). However, no reaction could be observed using 5-6 M TBHP in decane (entry 15, Table 1) which confirms the participation of H_2O as a source of proton transfer agent. Again, possibilities of classical disproportionation reactions of carbonyl compounds like Cannizzaro[43] and Tishchenko reactions[44] could be easily ruled out due to observation of aroyl radical intermediate. Thus, the mechanism of CRC reaction is identified

with the help of Cu(II) as catalyst. $Cu(OAc)_2.H_2O$ is a well-known oxidizing agent and probably caused over oxidation of aldehydes to acids in presence of more than 10 mol%. Hence, poor yield was observed with 20 mol% of Cu(II) (entry 4, Table 1).

In summary, we demonstrated Cu(II) catalyzed cross redox coupling (CRC) reaction for synthesis of esters directly from *p*-benzoquinone, and aldehydes (or alcohols) using TBHP-$Cu(OAc)_2.H_2O$ combination. This newly discovered CRC reaction of aldehydes and *p*-benzoquinone is also identified as an example of C-H functionalization of the aldehydes.[45] In this reaction none of the carbonyl compounds were pre-activated for esterification. Atom or electron economies were well conserved during the reaction. The proposed CRC methodology requires easily available precursors and can be performed on several aldehydes. We believe this reaction will lead to an important contribution in organic synthesis and mechanistic organic chemistry.

EXPERIMENTAL SECTION

General Methods. Column chromatographic purifications of the compounds were performed using silica gel (mesh 100–200) and hexane – ethyl acetate mixtures as eluent, unless otherwise specified. NMR spectra were recorded on a 400 MHz instrument at 25 °C. The chemical shift values are reported in parts per million (ppm) with respect to residual dimethyl sulfoxide (2.50 ppm for ^1H and 40.00 for ^{13}C). ^{13}C NMR spectra of all the compounds are recorded as proton-decoupled carbon spectra ($^{13}C\{^1H\}$). The peak patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; td, triplet of doublets; br s, broad singlet. The coupling constants (*J*) are reported in Hertz (Hz). High-resolution mass spectra (HR-MS) were recorded on an ESI-TOF (time of flight) mass spectrometer. Infrared

spectral data are reported in wave number (cm^{-1}). FT-IR spectra were recorded after making pellet of the compounds using anhydrous solid KBr. Melting points of the compounds were determined using a digital melting point apparatus and are uncorrected.

Caution. TBHP is a potential shock sensitive chemical.[37] Therefore, very high level of safety precautions should be exercised during reaction with TBHP. The precautions like PPEs (personal protective equipment) should be used while handling TBHP under neat condition. In this work, the TBHP was used as 70% in water. Use of blast shields is mandatory at all times during the reactions.

Yields (after column chromatography) were calculated based on recovered aldehydes. However, in parenthesis yields are calculated based on aldehydes used for the reaction.

Trapping of acyl radical by TEMPO: TEMPO (228 mg, 1.46 mmol, 2 equiv) was added to an oven-dried sealed tube charged with a magnetic stirring bar and **1b** (100 mg, 0.73 mmol, 1 equiv). $Cu(OAc)_2.H_2O$ (14.5 mg, 0.073 mmol, 10 mol %), and TBHP (0.3 mL, 2.2 mmol, 3 equiv, 70 % in water) were added to the mixture in DMSO, and the sealed tube was kept at 100 °C. The reaction was monitored by TLC. After completion of the reaction, the mass was dissolved in dichloromethane and purified by column chromatography to obtain 2,2,6,6-tetramethylpiperidin-1-yl-4-methoxybenzoate **(5)** . Yield 78% (166 mg); R_f 0.40 (2% diethyl ether/hexane); pale yellow liquid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.92 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H), 1.54 – 1.34 (m, 6H), 1.17 (s, 6H), 0.96 (s, 6H); ^{13}C{^{1}H}

NMR (100 MHz, DMSO-d_6) δ 165.6, 163.6, 131.5, 121.6, 114.6, 60.1, 55.9, 39.2, 32.0, 20.8, 16.9; IR Neat $\tilde{\nu}$ 2974, 2937, 1740, 1601, 1503, 1458, 1364, 1319, 1245, 1172, 1074, 1033, 922, 849, 771, 686, 608 cm^{-1}; HRMS observed 292.1907 (calculated for $C_{17}H_{26}NO_3$ $[M+H]^+$ 292.1913).

Procedure for preparation of 4-hydroxyphenyl-4-methoxybenzoate (3b): To an oven-dried sealed tube charged with a magnetic stirring bar and **1b** (100 mg, 0.73 mmol, 1 equiv), $Cu(OAc)_2.H_2O$ (14.5 mg, 0.073 mmol, 10 mol %), and TBHP (0.3 mL, 2.2 mmol, 3 equiv, 70 % in water) in DMSO (2 mL) was added **2** (120 mg, 1.1 mmol, 1.5 equiv). The reaction mixture was allowed to stir at 110 °C for 16 h. After cooling at room temperature, the reaction mixture washed with water and followed by extracted with ethyl acetate. Column purification using 15% ethyl acetate-hexane yielded **3b** 82% (117 mg, 66%) as pale yellow solid; R_f 0.20 (15% ethyl acetate/hexane); mp: 162-164 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.45 (s, 1H), 8.05 (d, J = 8.8 Hz, 1H), 7.10 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 165.0, 164.0, 155.5, 143.2, 132.3, 123.0, 121.7, 116.0, 114.7, 56.1; IR (KBr) $\tilde{\nu}$ 3438, 2935, 1701, 1597, 1509, 1398, 1321, 1287, 1261, 1168, 1112, 1073, 994, 850, 767, 696 cm^{-1}; HRMS observed 245.0808 (calculated for $C_{14}H_{13}O_4$ $[M+H]^+$ 245.0814).

Procedure for in situ oxidation of benzyl alcohols to aldehydes and preparation of 4-hydroxyphenyl-4-methoxybenzoate (3b): To an oven-dried sealed tube charged with a magnetic stirring bar and **4b** (100 mg, 0.72 mmol, 1 equiv), $Cu(OAc)_2.H_2O$ (14.5 mg, 0.072 mmol, 10 mol %), and TBHP (0.4 mL, 2.8 mmol, 4 equiv, 70 % in water) in DMSO (2 mL) was

added **2** (117 mg, 1.1 mmol, 1.5 equiv). The reaction mixture was allowed to stir at 110 °C for 20 h. After cooling at room temperature, the reaction mixture washed with water and followed by extracted with ethyl acetate. Column purification using 15% ethyl acetate-hexane yielded **3b** (104 mg, 73%) as pale yellow solid.

4-Hydroxyphenylbenzoate (3a): R_f 0.20 (10% ethyl acetate/hexane); colorless solid; yield 70% (90 mg, 58%) ; mp: 160-162 °C (lit.[46] 161-165 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.48 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 2H), 7.73 (t, *J* = 6.8 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 165.4, 155.6, 143.1, 134.3, 130.1, 129.6, 129.4, 123.0, 116.1; IR (KBr) $\tilde{\nu}$ 3455, 1714, 1596, 1508, 1398, 1338, 1281, 1209, 1188, 1112, 1066, 1000, 878, 816, 712 cm^{-1}; HRMS observed 215.0703 (calculated for $C_{13}H_{11}O_3$ $[M+H]^+$ 215.0709).

4-Hydroxyphenyl-4-methylbenzoate (3c): R_f 0.20 (10% ethyl acetate/hexane); off white solid; yield 65%, (93 mg, 49%); mp: 119-122 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.48 (s, 1H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.79 (d, *J* = 8.0 Hz, 2H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 165.3, 155.5, 144.7, 143.2, 130.1, 129.9, 126.8, 123.0, 116.0, 21.7; IR (KBr) $\tilde{\nu}$ 3331, 2919, 1721, 1709, 1601, 1507, 1395, 1286, 1181, 1114, 1080, 822, 747 cm^{-1}; HRMS observed 251.0677 (calculated for $C_{14}H_{12}O_3Na$ $[M+Na]^+$ 251.0679). .

4-Hydroxyphenyl-2-methylbenzoate (3d): R_f 0.20 (10% ethyl acetate/hexane); pale yellow solid; yield 63% (90 mg, 48%); mp: 114-116 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.47 (s, 1H),

8.02 (d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 2.57 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 166.2, 155.5, 143.1, 140.2, 133.1, 132.2, 131.0, 129.1, 126.6, 123.0, 116.0, 21.6; IR (KBr) $\tilde{\nu}$ 3436, 2962, 2929, 1719, 1593, 1507, 1446, 1392, 1249, 1209, 1180, 1053, 882, 824, 739, 596 cm^{-1}; HRMS observed 229.0887 (calculated for $C_{14}H_{13}O_3$ $[M+H]^+$ 229.0865).

4-Hydroxyphenyl-4-bromobenzoate (3e): R_f 0.20 (12% ethyl acetate/hexane); pale yellow solid; yield 60% (30 mg, 38%); mp: 126-127 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.52 (s, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 164.9, 155.8, 143.2, 132.7, 132.2, 129.0, 128.5, 123.1, 116.2; IR (KBr) $\tilde{\nu}$ 3373, 2922, 1730, 1590, 1509, 1458, 1398, 1287, 1207, 1114, 1077, 1009, 867, 848, 814, 749 cm^{-1}; HRMS observed 292.9808 (calculated for $C_{13}H_{10}BrO_3$ $[M+H]^+$ 292.9813).

4-Hydroxyphenyl-4-chlorobenzoate (3f): R_f 0.20 (12% ethyl acetate/hexane); colorless solid; yield 58% (62 mg, 35%); mp: 117-119 °C (lit.[46] 117 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.51 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.9 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 164.6, 155.7, 143.0, 139.2, 132.0, 129.6, 128.5, 122.9, 116.1; IR (KBr) $\tilde{\nu}$ 3379, 2933, 1730, 1592, 1510, 1486, 1399, 1292, 1208, 1111, 1075, 917, 850, 752 cm^{-1}; HRMS observed 249.0313 (calculated for $C_{13}H_{10}ClO_3$ $[M+H]^+$ 249.0319).

4-Hydroxyphenyl-2-ethylbenzoate (3g): R_f 0.20 (8% ethyl acetate/hexane); off white solid; yield 75% (101 mg, 56%); mp: 128-130 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.48 (s, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.42 - 7.36 (m, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 2.94 (q, *J* = 7.6 Hz, 2H), 1.19 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.4 , 155.6, 145.9, 143.1, 133.2, 130.9, 130.8, 129.0, 126.6, 123.0, 116.1, 27.2, 16.43; IR (KBr) $\tilde{\nu}$ 3466, 2960, 1705, 1598, 1520, 1446, 1397, 1254, 1180, 1066, 886, 820, 735, 587 cm^{-1}; HRMS observed 243.1016 (calculated for $C_{15}H_{15}O_3$ $[M+H]^+$ 243.1021).

4-Hydroxyphenyl-4-ethylbenzoate (3h): R_f 0.20 (8% ethyl acetate/hexane); off white solid; yield 72% (97 mg, 52%); mp: 120-122 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.49 (s, 1H), 8.01 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.21 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 165.4, 155.6, 150.8, 143.2, 130.3, 128.8, 127.1, 123.0, 116.1, 28.7, 15.7; IR (KBr) $\tilde{\nu}$ 3448, 2971, 2932, 1710, 1599, 1508, 1443, 1397, 1280, 1212, 1175, 1112, 1085, 881, 851, 822 cm^{-1}; HRMS observed 265.0835 (calculated for $C_{15}H_{14}O_3Na$ $[M+Na]^+$ 265.0841).

4-Hydroxyphenyl-3-bromo-4-methoxybenzoate (3i): R_f 0.22 (20% ethyl acetate/hexane); pale yellow solid; yield 75%, (89 mg, 59%); mp: 174-177 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.50 (s, 1H), 8.22 (d, *J* = 2.0 Hz, 1H), 8.10 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.8 Hz, 2H), 3.96 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 164.0, 160.1, 155.6, 143.1, 134.6, 131.8, 123.1, 123.0, 116.1, 113.1, 111.2, 57.3; IR (KBr) $\tilde{\nu}$ 3406, 2917, 2847, 1729, 1594, 1511, 1400, 1271, 1190, 1115, 1024, 1003, 829, 755 cm^{-1}; HRMS observed 322.9913 (calculated for $C_{14}H_{12}BrO_4$ $[M+H]^+$ 322.9919).

4-Hydroxyphenyl-2,4-dimethoxy-6-methylbenzoate (3j): R_f 0.24 (25% ethyl acetate/hexane); light orange solid; yield 85% (115 mg, 72%); mp: 112-114 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 (s, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.52 (s,1H), 6.49 (s, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.8, 161.8, 158.5, 155.5, 143.1, 138.0, 122.8, 116.1, 115.6, 107.5, 96.7, 56.4, 55.8, 19.8; IR (KBr) $\tilde{\nu}$ 3440, 2942, 2837, 1728, 1604, 1503, 1466, 1443, 1335, 1294, 1260, 1204, 1043, 746 cm^{-1}; HRMS observed 289.1071 (calculated for $C_{16}H_{17}O_5$ $[M+H]^+$ 289.1076).

4-Hydroxyphenyl-3,4-dimethoxybenzoate (3k): R_f 0.30 (25% ethyl acetate/hexane); light orange solid; yield 78% (103 mg, 63%); mp: 153-155 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 (s, 1H), 7.74 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H), 3.83 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 165.1, 155.5, 153.9, 149.0, 143.3, 124.3, 123.0, 121.6, 116.0, 112.5, 111.7, 56.2, 56.0; IR (KBr) $\tilde{\nu}$ 3440, 2917, 2847, 1740, 1601, 1510, 1417, 1274, 1191, 1139, 1078, 1012, 906, 755, 526 cm^{-1}; HRMS observed 275.0914 (calculated for $C_{15}H_{15}O_5$ $[M+H]^+$ 275.0919).

4-Hydroxyphenyl- 3,4,5-trimethoxybenzoate (3l): R_f 0.30 (30% ethyl acetate/hexane); light orange solid; yield 80% (98 mg, 64%); mp: 137-140 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.49 (s, 1H), 7.37 (s, 2H), 7.04 (d, *J* = 8.8 , 2H), 6.80 (d, *J* = 8.8, 2H), 3.86 (s, 6H), 3.76 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 165.0, 155.6, 153.3, 143.2, 142.7, 124.6, 123.0, 116.1, 107.5, 60.7, 56.5; IR (KBr) $\tilde{\nu}$ 3415, 2928, 2852, 1728, 1593, 1509, 1463, 1417, 1398, 1337,

1215, 1192, 1112, 1025, 996, 763, 702, 618 cm^{-1}; HRMS observed 305.1020 (calculated for $C_{16}H_{17}O_6$ $[M+H]^+$ 305.1025).

4-Hydroxyphenyl-2,4,6-trimethylbenzoate (3m): R_f 0.20 (12% ethyl acetate/hexane); colorless powder; yield 85% (116 mg, 67%); mp: 130-132 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.50 (s, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.98 (s, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 2.3 (s, 6H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.6, 155.7, 142.8, 139.8, 135.1, 130.5, 128.8, 122.8, 116.2, 21.2, 19.8; IR (KBr) $\tilde{\nu}$ 3469, 2928, 1723, 1596, 1508, 1444, 1398, 1264, 1207, 1177, 1112, 1066, 851, 809 cm^{-1}; HRMS observed 257.1192 (calculated for $C_{16}H_{17}O_3$ $[M+H]^+$ 257.1178).

4-Hydroxyphenyl-4-isopropylbenzoate (3n): R_f 0.22 (10% ethyl acetate/hexane); pale yellow solid; yield 76% (105 mg, 60%); mp: 115-119 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.47 (s, 1H), 8.02 (d, *J* = 8.4Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 3.00 (m,1H), 1.24 (d, *J* = 6.8 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 165.7, 155.7, 155.6, 143.5, 130.6, 127.6, 127.4, 123.3, 116.4, 34.3, 24.2; IR (KBr) $\tilde{\nu}$ 3375, 2962, 2933, 1713, 1593, 1509, 1397, 1276, 1193, 1112, 1075, 768, 705 cm^{-1}; HRMS observed 257.1203 (calculated for $C_{16}H_{17}O_3$ $[M+H]^+$ 257.1178).

4-Hydroxyphenyl-thiophene-2-carboxylate (3o): R_f 0.20 (10% ethyl acetate/hexane); brown solid; yield 68% (86 mg, 44%); mp: 109-111 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.51 (s, 1H), 8.06 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.98 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.29 (dd, *J* = 4.4, 3.6 Hz, 1H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 160.9,

155.7, 142.8, 135.4, 135.3, 132.6, 129.1, 123.0, 116.1; IR (KBr) $\tilde{\nu}$ 3448, 2923, 2852, 1691, 1594, 1505, 1408, 1291, 1260, 1205, 1183, 1112, 1067, 994, 917, 855, 807, 728 cm^{-1}; HRMS observed 221.0267 (calculated for $C_{11}H_9O_3S$ $[M+H]^+$ 221.0272).

4-Hydroxyphenyl-2-naphthoate (3p): R_f 0.22 (12% ethyl acetate/hexane); pale yellow solid; yield 74% (98 mg, 58%); mp: 138-142 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.52 (s, 1H), 8.80 (d, *J* = 8.4 Hz, 1H), 8.39 (d, *J* = 7.2 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.62 (m, 3H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 166.2, 155.7, 143.2, 134.5, 133.9, 131.2, 131.1, 129.3, 128.6, 127.0, 126.3, 125.5, 125.4, 123.1, 116.1; IR (KBr) $\tilde{\nu}$ 3412, 1696, 1592, 1505, 1433, 1401, 1343, 1282, 1245, 1128, 988, 882, 781 cm^{-1}; HRMS observed 265.0859 (calculated for $C_{17}H_{13}O_3$ $[M+H]^+$ 265.0865).

4-Hydroxyphenyl-anthracene-9-carboxylate (3q): R_f 0.30 (15% ethyl acetate/hexane); off white solid; yield 80% (110 mg, 71%); mp: 230-234 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.62 (s, 1H), 8.87 (s, 1H), 8.23 (d, *J* = 8.4 Hz, 2H), 8.17 (d, *J* = 8.8 Hz, 2H), 7.73-7.69 (m, 2H), 7.65 – 7.61 (m, 2H), 7.36 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.3, 156.0, 143.0, 130.9, 130.3, 129.3, 128.3, 128.0, 126.9, 126.4, 124.8, 123.1, 116.4; IR (KBr) $\tilde{\nu}$ 3500, 2934, 1730, 1597, 1507, 1447, 1401, 1270, 1197, 1171, 1115, 984, 874, 788 cm^{-1}; HRMS observed 337.0835 (calculated for $C_{21}H_{14}O_3Na$ $[M+Na]^+$ 337.0841).

4-Hydroxyphenyl-pyrene-1-carboxylate (3r): R_f 0.30 (15% ethyl acetate/hexane); bright yellow solid; yield 73% (80 mg, 55%); mp: 210-213 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.54

(s, 1H), 9.17 (d, *J* = 9.6 Hz, 1H), 8.84 (d, *J* = 8.4 Hz, 1H), 8.47-8.40(m, 5H), 8.32 (d, *J* = 9.6 Hz, 1H), 8.20 (t, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 166.7, 155.8, 143.5, 134.8, 131.07, 131.06, 130.6, 130.4, 130.3, 129.3, 127.7, 127.4, 127.1, 125.1, 124.6, 124.5, 123.8, 123.32 (×2), 122.8, 116.3; IR (KBr) $\tilde{\nu}$ 3432, 2927, 1683, 1586, 1500, 1440, 1324, 1226, 1174, 1129, 1076, 1035, 998, 889, 833, 709 cm^{-1}; HRMS observed 361.0835 (calculated for $C_{23}H_{14}O_3Na$ $[M+Na]^+$ 361.0841).

4-Hydroxy-3-(4-methoxybenzoyl)phenyl-4-methoxybenzoate (3b′): R_f 0.35 (8% ethyl acetate/hexane); pale yellow solid; yield 12 mg (<5%); mp: 188-191 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.28 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.15 (d, *J* = 2.8 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 194.8, 165.0, 164.2, 163.8, 153.9, 143.0, 132.5, 132.4, 130.2, 126.7, 126.1, 122.9, 121.5, 117.6, 114.7, 114.4, 56.18 , 56.13; IR (Neat) $\tilde{\nu}$ 3435, 2924, 2852, 1730, 1631, 1604, 1510, 1479, 1420, 1334, 1261, 1169, 1134, 1066, 1028, 970, 845, 785 cm^{-1}; HRMS observed 379.1184 (calculated for $C_{22}H_{18}O_6$ $[M+H]^+$ 379.1176).

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ASSOCIATED CONTENT

Supporting Information. ^{1}H, $^{13}C\{^{1}H\}$ NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

REFERENCES

(1) Huang, S.; Kotzner, L.; De, C. K.; List, B. *J. Am. Chem. Soc.* **2015**, *137*, 3446.

(2) Robinson, B. *Chem. Rev.* **1969**, *69*, 227.

(3) Robinson, B. *Chem. Rev.* **1963**, *63*, 373.

(4) Camp, C.; Mougel, V.; Horeglad, P.; Pécaut, J.; Mazzanti, M. *J. Am. Chem. Soc.* **2010**, *132*, 17374.

(5) Csaky, A. G.; Plumet, J. *Chem. Soc. Rev.* **2001**, *30*, 313.

(6) Paquette, L. A.; Moorhoff, C. M.; Maynard, G. D.; Hickey, E. R.; Rogers, R. D. *J. Org. Chem.* **1991**, *56*, 2449.

(7) Wang, P.; Tao, W. J.; Sun, X. L.; Liao, S.; Tang, Y. *J. Am. Chem. Soc.* **2013**, *135*, 16849.

(8) Abraham, I.; Joshi, R.; Pardasani, P.; Pardasani, R. T. *J. Braz. Chem. Soc.* **2011**, *22*, 385.

(9) Petrangolini, P.; Alessandrini, A.; Facci, P. *J. Phys. Chem. C* **2013**, *117*, 17451.

(10) Song, Y.; Buettner, G. R. *Free Radic. Biol. Med.* **2010**, *49*, 919.

(11) Gould, S. J. *Chem. Rev.* **1997**, *97*, 2499.

(12) Liu, J. K. *Chem. Rev.* **2006**, *106*, 2209.

(13) Schaffner, A.-P.; Renaud, P. *Eur. J. Org. Chem.* **2004**, 2291.

(14) Overeem, J. C. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 684.

(15) Mothe, S. R.; Susanti, D.; Chan, P. W. H. *Tetrahedron Lett.* **2010**, *51*, 2136.

(16) Walker, S. E.; Jordan-Hore, J. A.; Johnson, D. G.; Macgregor, S. A.; Lee, A. L. *Angew. Chem. Int. Ed. Engl.* **2014**, *53*, 13876.

(17) Deb, A.; Manna, S.; Maji, A.; Dutta, U.; Maiti, D. *Eur. J. Org. Chem.* **2013**, 5251.

(18) Wang, D.; Ge, B.; Li, L.; Shan, J.; Ding, Y. *J. Org. Chem.* **2014**, *79*, 8607.

(19) Collet, F.; Lescot, C.; Dauban, P. *Chem. Soc. Rev.* **2011**, *40*, 1926.

(20) McNally, A.; Haffemayer, B.; Collins, B. S. L.; Gaunt, M. J. *Nature* **2014**, *510*, 129.

(21) Sharma, A.; Hartwig, J. F. *Nature* **2015**, *517*, 600.

(22) Schranck, J.; Tlili, A.; Beller, M. *Angew. Chem. Int. Ed. Engl.* **2014**, *53*, 9426.

(23) He, J.; Li, S.; Deng, Y.; Fu, H.; Laforteza, B. N.; Spangler, J. E.; Homs, A.; Yu, J.-Q. *Science* **2014**, *343*, 1216.

(24) Studer, A.; Curran, D. P. *Angew. Chem. Int. Ed.* **2011**, *50*, 5018.

(25) Engelman, K. L.; Feng, Y.; Ison, E. A. *Organometallics* **2011**, *30*, 4572.

(26) Karakaya, I.; Primer, D. N.; Molander, G. A. *Org. Lett.* **2015**, *17*, 3294.

(27) Minakawa, M.; Baek, H.; Yamada, Y. M. A.; Han, J. W.; Uozumi, Y. *Org. Lett.* **2013**, *15*, 5798.

(28) Wang, Y.; Aleiwi, B. A.; Wang, Q.; Kurosu, M. *Org. Lett.* **2012**, *14*, 4910.

(29) Procopiou, P. A.; Baugh, S. P. D.; Flack, S. S.; Inglis, G. G. A. *J. Org. Chem.* **1998**, *63*, 2342.

(30) Dev, D.; Palakurthy, N. B.; Thalluri, K.; Chandra, J.; Mandal, B. *J. Org. Chem.* **2014**, *79*, 5420.

(31) Ishihara, K.; Nakagawa, S.; Sakakura, A. *J. Am. Chem. Soc.* **2005**, *127*, 4168.

(32) Yoo, W.-J.; Li, C.-J. *J. Org. Chem.* **2006**, *71*, 6266.

(33) Kumar, G. S.; Maheswari, C. U.; Kumar, R. A.; Kantam, M. L.; Reddy, K. R. *Angew. Chem. Int. Ed.* **2011**, *50*, 11748.

(34) Xia, J.; Shao, A.; Tang, S.; Gao, X.; Gao, M.; Lei, A. *Org. Biomol. Chem.* **2015**, *13*, 6154.

(35) Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F. *Nature* **2014**, *510*, 485.

(36) Molina, M. T.; Navarro, C.; Moreno, A.; Csaky, A. G. *J. Org. Chem.* **2009**, *74*, 9573.

(37) Achar, T. K.; Mal, P. *J. Org. Chem.* **2015**, *80*, 666.

(38) Wessjohann, L. A.; Rivera, D. G.; Vercillo, O. E. *Chem. Rev.* **2009**, *109*, 796.

(39) Liu, Z.; Zhang, J.; Chen, S.; Shi, E.; Xu, Y.; Wan, X. *Angew. Chem. Int. Ed.* **2012**, *51*, 3231.

(40) Rout, S. K.; Guin, S.; Banerjee, A.; Khatun, N.; Gogoi, A.; Patel, B. K. *Org. Lett.* **2013**, *15*, 4106.

(41) Zhao, J.; Fang, H.; Han, J.; Pan, Y. *Org. Lett.* **2014**, *16*, 2530.

(42) Kumli, E.; Montermini, F.; Renaud, P. *Org. Lett.* **2006**, *8*, 5861.

(43) Curini, M.; Epifano, F.; Genovese, S.; Marcotullio, M. C.; Rosati, O. *Org. Lett.* **2005**, *7*, 1331.

(44) Mojtahedi, M. M.; Akbarzadeh, E.; Sharifi, R.; Abaee, M. S. *Org. Lett.* **2007**, *9*, 2791.

(45) Yang, L.; Huang, H. *Chem. Rev.* **2015**, *115*, 3468.

(46) Panchgalle, S. P.; Kalkote, U. R.; Niphadkar, P. S.; Joshi, P. N.; Chavan, S. P.; Chaphekar, G. M. *Green Chem.* **2004**, *6*, 308.