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Note

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Tuning Regioselectivity of Wacker Oxidation in One Catalytic System: Small Change Makes Big Step

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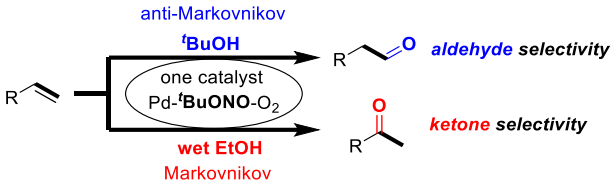
Supporting Information Placeholder



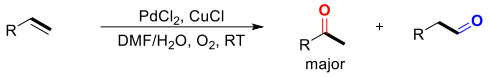
ABSTRACT: A regioselectivity switchable aerobic Wacker–Tsuji oxidation has been developed using catalytic *tert*-butyl nitrite as a simple organic redox cocatalyst. By solely switching the solvent, either substituted aldehydes or ketones could be prepared under mild aerobic conditions in good yields, respectively. A mechanistic explanation for the selectivity control is proposed.

The oxidation of terminal olefins to carbonyl compounds with palladium(II) chloride and copper(I) chloride in the presence of air, known as Wacker-Tsuji oxidation,[1] has proven to be a powerful tool in synthetic chemistry due to its practicability, efficiency and broad functional group compatibility (Scheme 1).[2-4] Traditional Wacker-Tsuji oxidation usually proceeds in wet DMF, which follows Markovnikov's rule to yield ketones as the major products, whereas the *anti*-Markovnikov selective oxidation for the direct synthesis of aldehyde is highly desirable and attracted a lot of research interest.[5-9] The *anti*-Markovnikov oxidation has been realized by the using directing of functional group on the olefins[6] or steric effects of solvents.[5] Thus, different strategies or methods have been applied to accomplish ketones or aldehydes.

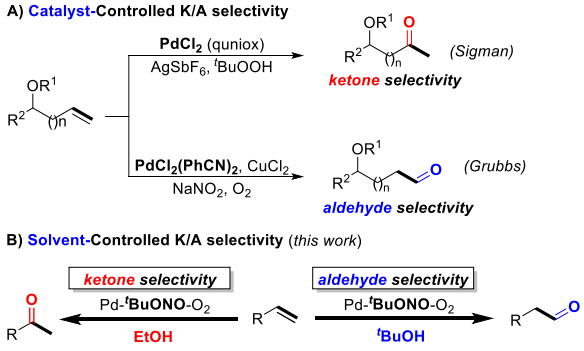
The switch of such selectivity solely via tiny change of the reaction conditions in one catalytic system would be very valuable to achieve different targets for different purposes in organic synthesis. However, the development of regioselectivity-switchable Wacker-Tsuji oxidation has always been a challenge. The ketone-selective Wacker oxidation is a thermodynamic controlled Markovnikov process, whereas the aldehyde-selectivity is kinetically controlled *anti*-Markovnikov process. Even several individual examples have been involved with the accomplishment of the ketone-[3] or aldehyde-selective[8] Wacker oxidation; there are few examples on the efficient control of the regioselectivity of Wacker oxidation (Scheme 2A).

In our research concerning ammoxidation of methylarenes,[10b] we noticed that ^{t}BuONO was a convenient organic NO-source which might replace inorganic NO_2-salts[10c] in catalysis. We then developed an aldehyde-selective aerobic Wacker–Tsuji oxidation using *tert*-butyl nitrite as a simple organic redox cocatalyst.[10a] During our investigations, we found that the solvent is crucial to the regioselectivity control of aerobic Wacker-Tsuji oxidation. After careful studies, we realized a ketone/aldehyde selectivity controllable Wacker-Tsuji oxidation by just switching solvent (Scheme 2B). Herein we present this result in details.

Scheme 1. Wacker-Tsuji Oxidation Catalyzed by Pd-Cu System

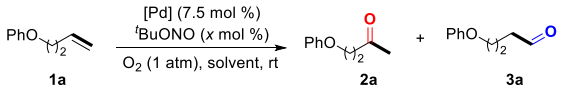


Scheme 2. Site-Selectivity Control with One Catalytic System



We first choose (but-3-en-1-yloxy)benzene **1a** as model substrate in the aerobic oxidation with ^{t}BuONO as a redox cocatalyst using $Pd(PhCN)_2Cl_2$ as catalyst to investigate various solvents (Table 1, entries 1-5). When ^{t}BuOH was used, aldehyde product **3a** was obtained in 80% yield with 15% ketone product **2a** (entry 1). Yield of aldehyde **3a** decreases as the substituent on alcohol becomes smaller (entries 2-5). But EtOH gives the highest yield of ketone **2a** (entry 4). The addition of water (2.0 equivalent) suppresses aldehyde product **3a** and improves the yield of ketone **2a** to 76% (entry 4 vs 6). Reducing the loading of ^{t}BuONO results in the decreased yield of **2a** (entries 7-8), while increasing the loading of ^{t}BuONO does not affect the yield of **2a** (entries 9-11). Other catalyst, such as $Pd(CH_3CN)_2Cl_2$, $PdCl_2$, $Pd(OAc)_2$, were also employed but did not improve of yield of **2a** (entries 12-14).

Table 1. Reaction Conditions[a]

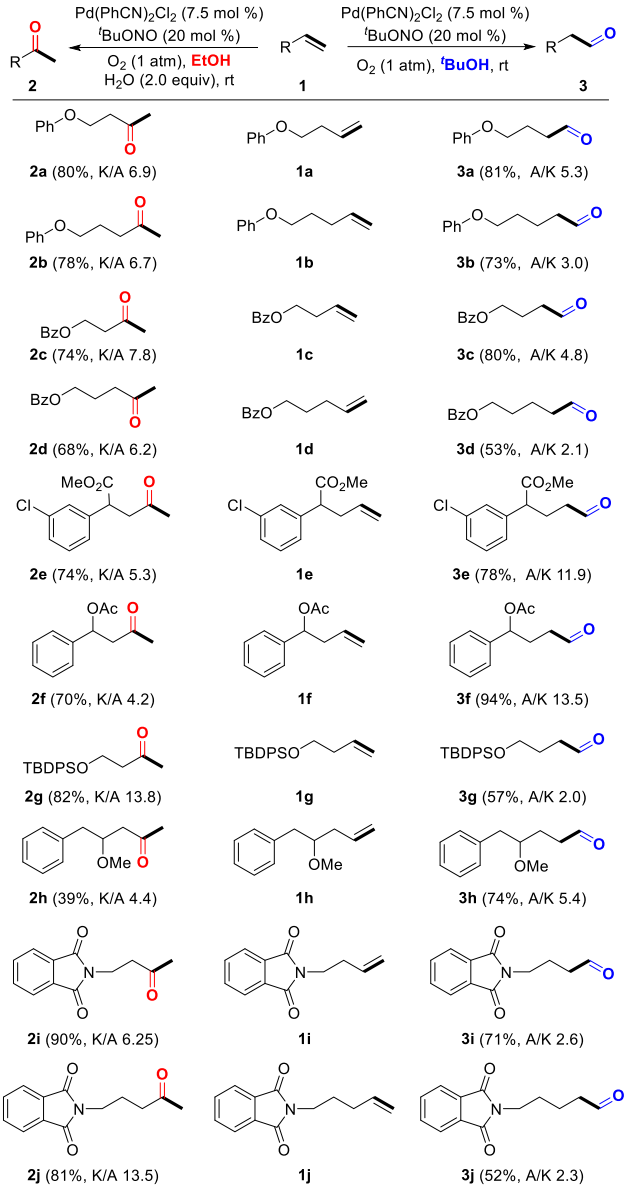


entry	[Pd]	x	solvent	t(h)	2a[b]	3a[b]
1	$Pd(PhCN)_2Cl_2$	20	^{t}BuOH	1	15	80
2	$Pd(PhCN)_2Cl_2$	20	^{n}BuOH	11	36	64
3	$Pd(PhCN)_2Cl_2$	20	^{i}PrOH	1	55	45
4	$Pd(PhCN)_2Cl_2$	20	EtOH	1	67	30
5	$Pd(PhCN)_2Cl_2$	20	MeOH	1	44	23
6[c]	$Pd(PhCN)_2Cl_2$	20	EtOH	0.5	76	24
7[c]	$Pd(PhCN)_2Cl_2$	0	EtOH	24	6	trace
8[c]	$Pd(PhCN)_2Cl_2$	10	EtOH	1.5	61	36
9[c]	$Pd(PhCN)_2Cl_2$	30	EtOH	0.5	75	25
10[c]	$Pd(PhCN)_2Cl_2$	50	EtOH	0.5	77	23
11[c]	$Pd(PhCN)_2Cl_2$	100	EtOH	0.5	74	21
12[c]	$Pd(CH_3CN)_2Cl_2$	20	EtOH	2	61	23
13[c]	$PdCl_2$	20	EtOH	24	55	11
14[c]	$Pd(OAc)_2$	20	EtOH	24	20	trace

[a] Reaction conditions: **1a** (0.5 mmol), solvent (2 mL). [b] **2a**/**3a** was determined by ^{1}H NMR using CH_3NO_2, ^{t}BuOMe as internal standard. [c] H_2O (2.0 equiv) was used as additive.

After establishing the optimized reaction conditions (7.5 mol % of $Pd(PhCN)_2Cl_2$, 20 mol % ^{t}BuONO, using either ^{t}BuOH or EtOH as solvent), the scope of ketone/aldehyde-selectivity switchable Wacker–Tsuji oxidation is evaluated (Scheme 3). Various terminal alkenes bearing different functional groups were subjected to the optimized conditions and ketone **2** and aldehyde **3** were obtained with as high as 13.8:1 regioselectivity in generally good to high isolated yields. Various functional groups or protecting groups could be tolerated under this reaction conditions. For example, ketone **2b** and aldehyde **3b** bearing phenyl ether groups were isolated in 78% and 73% yields with good regioselectivity. The ester groups are tolerated in this reaction (**2c-f** and **3c-f**). The ether protecting groups such as TBDPS and methyl group kept unchanged in this oxidation (**2g–h** and **3g–h**). Even nitrogen-containing substrates reacted smoothly giving the desired ketones and aldehydes in up to 90% yields and up to 13.5:1 selectivity (**2i–j**, and **3i–j**). A drawback for this method is that styrene and 1-octene are not suitable for aldehyde-selectivity and only ketone products are obtained.

Scheme 3. Reaction Scope[a]

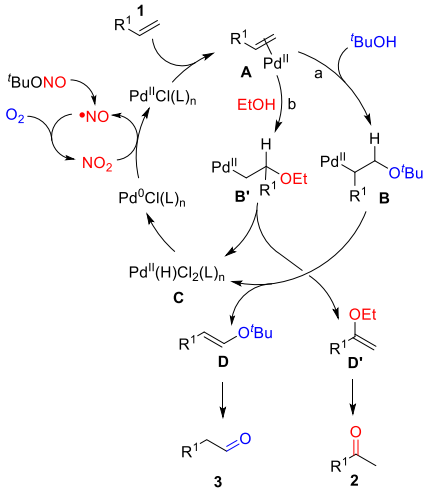


[a] Conditions: **1** (0.5 mmol), $Pd(PhCN)_2Cl_2$ (7.5 mol %), ^{t}BuONO (20 mol %), ^{t}BuOH (2 mL) or EtOH (2 mL with 2 equiv H_2O), O_2 (1 atm). Ratio (K/A or A/K) refers to **A**ldehyde and **K**etone.

A plausible mechanism for site-selectivity switchable Wacker–Tsuji oxidation is proposed (Scheme 4). Pd(II) coordinates with alkene **1** to form intermediate **A** which is attacked by the alcohol solvent to generate intermediate **B**. The β–elimination affords enol ether **D** or **D'**. For bulky solvent ^{t}BuOH aldehyde **3** is obtained whereas for smaller alcohol EtOH ketone **2** is achieved. Catalytically active Pd(II) species is regenerated by the oxidation of NO_2 which is in

situ produced from the oxidation of NO with molecular oxygen. ^{t}BuONO is the donor of NO and thus plays the role of redox cocatalyst.

Scheme 4. Proposed Mechanism



In conclusion, we have developed regioselectivity controllable aerobic Wacker–Tsuji oxidation at room temperature under copper- or silver-free conditions. Catalytic amount of *tert*-butyl nitrite worked as a simple organic redox cocatalyst. A variety of aldehydes and ketones were achieved in generally high regioselectivity as well as good to high yields.

EXPERIMENTAL SECTION

General Information. Solvents were pre-dried over activated MS 4Å and heated to reflux over sodium (for toluene and THF) or calcium hydride (for CH_2Cl_2) under a nitrogen atmosphere and collected by distillation. ^{1}H NMR (400 MHz) and ^{13}C{^{1}H} NMR (100 MHz) spectra were recorded on a Bruker spectrometer. Chemical shifts are reported in δ units relative to (TMS, ^{1}H δ = 0; $CDCl_3$, ^{1}H δ = 7.26, ^{13}C δ = 77.36).

General procedure for Markovnikov selective Wacker oxidation under Pd-^{t}BuONO-O_2-system in wet EtOH. $Pd(PhCN)_2Cl_2$ (14.4 mg, 0.0375 mmol) was weighed directly into a 25 mL Schlenk tube and dried under high vacuum for 20 min. Under an atmosphere of oxygen (1 atm, balloon), EtOH (2 mL), H_2O (1.0 mmol) and ^{t}BuONO (10.3 mg, 0.1 mmol) were added and stirred at 25 °C. Alkene (0.5 mmol) was then added and the resulting reaction mixture was monitored by TLC. After completion, the reaction was quenched by addition of water (5 mL) and extracted three times with CH_2Cl_2. The combined organic layers were subsequently washed with brine and dried over Na_2SO_4. The organic solvent was removed under reduced pressure then the crude mixture was examined on ^{1}H NMR spectrometer to determine the conversion and selectivity using *tert*-butyl methyl ether (with nitromethane as a dual standard) as internal standard. The crude product was purified by chromatography on silica gel to afford the corresponding products.

4-phenoxybutan-2-one ***(2a)***.[10a] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 40/1), yellow oil, 65.7 mg, 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2 H), 6.96 (d, *J* = 7.2 Hz, 1 H), 6.93-6.89 (m, 2 H), 4.23 (t, *J* = 6.4 Hz, 2 H), 2.91 (t, *J* = 6.4 Hz, 2 H), 2.25 (s, 3 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.8, 158.9, 129.8, 121.3, 114.9, 63.1, 43.3, 30.9.

5-phenoxypentan-2-one ***(2b)***.[11] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 40/1), as yellow solid(69.5 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.28 (m, 2 H), 6.94 (t, *J* = 7.2 Hz, 1 H), 6.88 (d, *J* = 8.0 Hz, 2 H), 3.97 (t, *J* = 6.0 Hz, 2 H), 2.66 (t, *J* = 7.2 Hz, 2 H), 2.18 (s, 3 H), 2.09-2.03 (m, 2 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 208.7, 159.1, 129.8, 121.0, 114.7, 66.9, 40.3, 30.4, 23.7.

3-oxobutyl benzoate ***(2c)***.[12] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 20/1), yellow oil, 71.1mg, 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.6 Hz, 2 H), 7.55 (t, *J* = 7.6 Hz, 1 H), 7.42 (t, *J* = 7.6 Hz, 2 H), 4.58 (t, *J* = 6.0 Hz, 2 H), 2.90 (t, *J* = 6.0 Hz, 2 H), 2.23 (s, 3 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.0, 166.7, 133.4, 130.3, 129.9, 128.7, 60.1, 42.7, 30.6.

4-oxopentyl benzoate ***(2d)***.[13] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 20/1), as yellow oil (70.4 mg, 68%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 2 H), 7.56 (t, *J* = 7.6 Hz, 1 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 4.33 (t, *J* = 6.4 Hz, 2 H), 2.60 (t, *J* = 7.0 Hz, 2 H), 2.17 (s, 3 H), 2.09-2.02 (m, 2 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 208.1, 166.9, 133.3, 130.5, 129.9, 128.7, 64.4, 40.3, 30.4, 23.2.

methyl 2-(3-chlorophenyl)-4-oxopentanoate ***(2e)***. This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 20/1), yellow oil, 86.4 mg, 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.26 (m, 3 H), 7.16 (s, 1 H), 4.09 (dd, *J* = 10.0, 4.0 Hz, 1 H), 3.68 (s, 3 H), 3.39 (dd, *J* = 18.0, 10.0 Hz, 1 H), 2.73 (dd, *J* = 18.0, 4.0 Hz, 1 H), 2.20 (s, 3 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.0, 173.5, 140.3, 134.9, 130.4, 128.2, 128.1, 126.4, 52.8, 47.1, 46.0, 30.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{13}ClO_3Na$ 263.0451; Found 263.0454.

3-oxo-1-phenylbutyl acetate ***(2f)***.[14] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 10/1), as yellow oil (72.2 mg, 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.32 (m, 3 H), 7.31-7.29 (m, 1 H), 6.18 (dd, *J* = 8.8, 5.2 Hz, 1 H), 3.12 (dd, *J* = 16.8, 8.8 Hz, 1 H), 2.82 (dd, *J* = 16.8, 5.2 Hz, 1 H), 2.15 (s, 3 H), 2.03 (s, 3 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 204.8, 170.0, 139.8, 128.8, 128.4, 126.6, 71.7, 50.0, 30.6, 21.2.

4-((tert-butyldiphenylsilyl)oxy)butan-2-one ***(2g)***. This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 40/1), as yellow oil (133.9 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.0, 1.6 Hz, 4 H), 7.45−7.37 (m, 6 H), 3.94 (t, *J* = 6.4 Hz, 2 H), 2.64 (t, *J* = 6.4 Hz, 2 H), 2.19 (s, 3 H), 1.03 (s, 9 H).^{13}C NMR (100 MHz, $CDCl_3$) δ 208.3, 135.9, 133.8, 130.1, 128.1, 60.0, 46.7, 31.1, 27.1, 19.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{26}O_2Si$ 349.1600; Found 349.1598.

4-methoxy-5-phenylpentan-2-one ***(2h)***.[15] This compound was prepared according to the general procedure,

$Pd(PhCN)_2Cl_2$ (14.4 mg, 0.0375 mmol), purified by flash column chromatography (PE/EA = 10/1), as colorless oil (37.5 mg, 39%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.2 Hz, 2 H), 7.23 (d, *J* = 7.2 Hz, 1 H), 7.19 (d, *J* = 7.2 Hz, 2 H), 3.95-3.89 (m, 1 H), 3.34 (s, 3 H), 2.91 (dd, *J* = 13.6, 6.0 Hz, 1 H), 2.72 (dd, *J* = 13.6, 6.8 Hz, 1 H), 2.62 (dd, *J* = 16.4, 8.0 Hz, 1 H), 2.41 (dd, *J* = 16.0, 4.4 Hz, 1 H), 2.12 (s, 3 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 207.7, 138.3, 129.8, 128.8, 126.7, 78.6, 57.7, 48.0, 40.1, 31.4.

*2-(3-oxobutyl) isoindoline-1,3-dione (**2i**).*[16] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 10/1), as a yellow solid (97.7 mg, 90%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85−7.83 (m, 2 H), 7.73−7.70 (m, 2 H), 3.95 (t, *J* = 7.4 Hz, 2 H), 2.87 (t, *J* = 7.4 Hz, 2 H), 2.18 (s, 3 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.2, 168.4, 134.3, 132.4, 123.6, 41.9, 33.3, 30.3.

*2-(4-oxopentyl) isoindoline-1,3-dione (**2j**).*[17] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 10/1), as white solid (89 mg, 81%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86-7.81 (m, 2 H), 7.73-7.69 (m, 2 H), 3.70 (t, *J* = 6.6 Hz, 2 H), 2.49 (t, *J* = 7.2 Hz, 2 H), 2.13 (s, 3 H), 1.94-1.91 (m, 2 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 207.8, 168.8, 134.3, 132.3, 123.5, 40.8, 37.4, 30.2, 22.9.

General procedure for *anti*-Markovnikov Wacker oxidation under Pd-^{t}BuONO-O_2-system in ^{t}BuOH. $Pd(PhCN)_2Cl_2$ (14.4 mg, 0.0375mmol) was weighed directly into a 25 mL Schlenk tube and dried under high vacuum for 20 mins. Under an atmosphere of oxygen (1 atm, balloon), ^{t}BuOH (2 mL) and ^{t}BuONO (10.3 mg, 0.1 mmol) were added and stirred at 25 °C. Alkene (0.5 mmol) was then added and the resulting reaction mixture was monitored by TLC. After completion, the reaction was quenched by addition of water (5 mL) and extracted three times with CH_2Cl_2. The combined organic layers were subsequently washed with brine and dried over Na_2SO_4. The organic solvent was removed under reduced pressure then the crude mixture was examined on ^1H NMR spectrometer to determine the conversion and selectivity using *tert*-butyl methyl ether (with nitromethane as a dual standard) as internal standard. The crude product was purified by chromatography on silica gel to afford the corresponding products.

*4-phenoxybutanal (**3a**).*[8a] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 40/1), as yellow oil (66.9 mg, 81%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1 H), 7.33 (t, *J* = 7.8 Hz, 2 H), 6.97 (t, *J* = 7.4 Hz, 1 H), 6.90 (d, *J* = 8.0 Hz, 2 H), 4.02 (t, *J* = 5.8 Hz, 2 H), 2.69 (t, *J* = 7.0 Hz, 2 H), 2.18-2.11 (m, 2 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 202.2, 158.9, 129.8, 121.1, 114.7, 66.8, 40.9, 22.3.

*5-phenoxypentanal (**3b**).*[18] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 40/1), as yellow oil (65.1 mg, 73%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1 H), 7.32-7.28 (m, 2 H), 6.98-6.94 (m, 1 H), 6.91 (d, *J* = 8.0 Hz, 2 H), 3.99 (t, *J* = 5.6 Hz, 2 H), 2.55 (t, *J* = 6.0 Hz, 2 H), 1.85 (s, 4 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 202.7, 159.2, 129.8, 121.0, 114.7, 67.5, 43.8, 29.0, 19.1.

*4-oxobutyl benzoate (**3c**).*[19] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 10/1), yellow oil, 76.9 mg, 80%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1 H), 8.02 (d, *J* = 7.2 Hz, 2 H), 7.59-7.55 (m, 1 H), 7.47-7.43 (m, 2 H), 4.37 (t, *J* = 6.2 Hz, 2 H), 2.65 (t, *J* = 6.8 Hz, 2 H), 2.16-2.09 (m, 2 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.5, 166.8, 133.4, 129.9, 128.7, 64.2, 40.9, 21.8.

*5-oxopentyl benzoate (**3d**).*[20] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 20/1), as colorless oil (50.9 mg, 53%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1 H), 8.04-8.02 (m, 2 H), 7.58-7.54 (m, 1 H), 7.46-7.42 (m, 2 H), 4.34 (t, *J* = 5.6 Hz, 2 H), 2.54 (t, *J* = 5.8 Hz, 2 H), 1.82-1.81 (m, 4 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ202.3, 166.9, 133.3, 130.6, 129.9, 128.7, 64.7, 43.7, 28.5, 19.0.

*methyl 2-(3-chlorophenyl)-5-oxopentanoate (**3e**).* This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 10/1), yellow oil, 94.2 mg, 78%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1 H), 7.29−7.28 (m, 3 H), 7.18 (s, 1 H), 3.69 (s, 3 H), 3.61 (t, *J* = 7.6 Hz, 1 H), 2.45 (t, *J* = 7.0 Hz, 2 H), 2.40-2.35 (m, 1 H), 2.15-2.08 (m, 1 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.4, 173.7, 140.4, 135.0, 130.4, 128.4, 128.2, 126.5, 52.6, 50.2, 41.6, 25.8. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{13}ClO_3Na$ 263.0451; Found 263.0451.

*4-oxo-1-phenylbutyl acetate (**3f**).*[10a] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 10/1), as yellow oil (97.1 mg, 94%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1 H), 7.37-7.31 (m, 5 H), 5.77 (t, *J* = 6.8 Hz, 1 H), 2.47 (t, *J* = 7.4 Hz, 2 H), 2.27-2.12 (m, 2 H), 2.08 (s, 3 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.3, 170.5, 140.0, 128.9, 128.5, 126.6, 75.2, 40.2, 28.9, 21.4.

*4-((tert-butyldiphenylsilyl)oxy)butanal (**3g**).*[10a] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 40/1), as yellow oil (93.2 mg, 57%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1 H), 7.66-7.64 (m, 4 H), 7.45-7.37 (m, 6 H), 3.69 (t, *J* = 6.0 Hz, 2 H), 2.55 (t, *J* = 7.2 Hz, 2 H), 1.92-1.86 (m, 2 H), 1.04 (s, 9 H) $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 203.0, 135.9, 133.9, 130.0, 128.0, 63.2, 41.1, 27.1, 25.6, 19.4.

*4-methoxy-5-phenylpentanal (**3h**).* This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 20/1), as yellow oil (71.2 mg, 74%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.72 (t, *J* = 1.6 Hz, 1 H), 7.32-7.28 (m, 2 H), 7.24-7.18 (m, 3 H), 3.41-3.35 (m, 1 H), 3.30 (s, 3 H), 2.93 (dd, *J* = 13.8, 5.8 Hz, 1 H), 2.67 (dd, *J* = 13.8, 6.8 Hz, 1 H), 2.48 (tt, *J* = 7.4, 1.6 Hz, 2 H), 1.88-1.80 (m, 1 H), 1.76-1.67 (m, 1 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 202.3, 138.3, 129.4, 128.4, 126.3, 81.5, 57.0, 40.1, 40.0, 26.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{16}O_2Na$ 215.1048; Found 215.4052.

*4-(1, 3-dioxoisoindolin-2-yl)butanal (**3i**).*[21] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 10/1), as yellow oil (76.7 mg, 71%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1 H), 7.87-7.83 (m, 2 H), 7.74-7.71 (m, 2 H), 3.74 (t, *J* = 6.8 Hz, 2 H), 2.54 (t, *J* = 6.8 Hz, 2 H), 2.05-1.98 (m, 2 H). $^{13}C\{^1H\}$ NMR

(100 MHz, $CDCl_3$) δ 201.2, 168.7, 134.4, 132.3, 123.6, 41.4, 37.4, 21.5.

*5-(1, 3-dioxoisoindolin-2-yl) pentanal (**3j**).*[22] This compound was prepared according to the general procedure, purified by flash column chromatography (PE/EA = 10/1), as colorless oil (60.1 mg, 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1 H), 7.85-7.82 (m, 2 H), 7.73-7.70 (m, 2 H), 3.71 (t, *J* = 6.6 Hz, 2 H), 2.50 (t, *J* = 6.6 Hz, 2 H), 1.77-1.65 (m, 4 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 202.2, 168.8, 134.3, 132.4, 123.6, 43.5, 37.8, 28.3, 19.5.

General procedures for homoallylation of phenols and amines (1a, 1b, 1i, and 1j). To a solution of an aromatic alcohol or amine (10 mmol) and K_2CO_3 (20 mmol) in CH_3CN (30 mL) was added 4-bromo-1-butene (2.0 mL, 15 mmol), and the mixture was refluxed for 12 h. The reaction mixture was concentrated, and the residue was partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL), dried over anhydrous Na_2SO_4, and concentrated in *vacuo*. The resulting residue was purified by silica gel flash chromatography to provide the titled compounds.

*(but-3-en-1-yloxy)benzene (**1a**).*[23] This compound was prepared according to general procedure and purified by silica gel column (PE/EA = 20/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.28 (m, 2 H), 6.99-6.97 (m, 1 H), 6.95-6.93 (m, 2 H), 6.00-5.89 (m, 1 H), 5.23-5.13 (m, 2 H), 4.05 (t, *J* = 6.8 Hz, 2 H), 2.58 (q, *J* = 6.8 Hz, 2 H).

*(pent-4-en-1-yloxy)benzene (**1b**).*[24] This compound was prepared according to general procedure and purified by silica gel column (PE/EA = 20/1): 0.81 g, 50%, yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 (t, *J* = 7.6 Hz, 2 H), 6.95-6.89 (m, 3 H), 5.90-5.80 (m, 1 H), 5.08-4.99 (m, 2 H), 3.96 (t, *J* = 6.4 Hz, 2 H), 2.24 (q, *J* = 7.2 Hz, 2 H), 1.92-1.85 (m, 2 H).

*2-(but-3-en-1-yl)isoindoline-1,3-dione (**1i**).*[25] This compound was prepared according to general procedure and purified by silica gel column (PE/EA = 10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85-7.81 (m, 2 H), 7.72-7.68 (m, 2 H), 5.84-5.74 (m, 1 H), 5.08-5.00 (m, 2 H), 3.77 (t, *J* = 6.8 Hz, 2 H), 2.44 (q, *J* = 6.8 Hz, 2 H).

*2-(pent-4-en-1-yl)isoindoline-1,3-dione (**1j**).*[23] This compound was prepared according to general procedure and purified by silica gel column (PE/EA = 10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.82 (m, 2 H), 7.73-7.69 (m, 2 H), 5.87-5.77 (m, 1 H), 5.07-4.96 (m, 2 H), 3.70 (t, *J* = 7.2 Hz, 2 H), 2.12 (q, *J* = 7.2 Hz, 2 H), 1.82-1.75 (m, 2 H).

General procedure for synthesis of starting materials (1c-1d). 4-Penten-1-ol (0.86 g, 10 mmol) and pyridine (0.95 g, 12mmol) were dissolved in 20 mL dry DCM. Benzoyl chloride (2.12 g, 12 mmol) was then added dropwise to the solution at 0 °C. The resulting reaction mixture was allowed to warm up to rt and was stirred for 1 h. The insoluble salt was filtered and the solvent was removed in *vacuo*. The residue was purified by flash column chromatography(silica gel, PE:EA = 100:1) to afford the titled product.

*but-3-en-1-yl benzoate (**1c**).*[26] This compound was prepared according to general procedure and purified by silica gel column (PE/EA = 100/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 6.8 Hz, 2 H), 7.57-7.54 (m, 1 H), 7.46-7.42 (m, 2 H), 5.93-5.83 (m, 1 H), 5.20-5.10 (m, 2 H), 4.38 (t, *J* = 6.6 Hz, 2 H), 2.56-2.51 (m, 2 H).

*pent-4-en-1-yl benzoate (**1d**).*[27] This compound was prepared according to general procedure and purified by silica gel column (PE/EA = 100/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.2 Hz, 2 H), 7.58-7.54 (m, 1 H), 7.46-7.42 (m, 2 H), 5.90-5.80 (m, 1 H), 5.10-5.00 (m, 2 H), 4.34 (t, *J* = 6.4 Hz, 2 H), 2.25-2.20 (m, 2 H), 1.91-1.84 (m, 2 H).

*methyl 2-phenylpent-4-enoate (**1e**).* This compound was prepared in 70% yield according to the literature method.[28] ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33-7.27 (m, 1 H), 7.26-7.20(m, 3 H), 5.76-5.66 (m, 1 H), 5.11-5.02 (m, 2 H), 3.69 (s, 3 H), 3.64 (t, *J* = 7.6 Hz, 2 H), 2.86-2.79 (m. 1 H), 2.55-2.48 (m, 1 H).

*1-phenylbut-3-en-1-yl acetate (**1f**).* This compound was prepared in 85% yield as a colorless oil according to the literature method.[10a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (m, 5 H), 5.82-5.79 (m, 1 H), 5.75-5.65 (m, 1 H), 5.10-5.03 (m, 2 H), 2.69-2.52 (m, 2 H), 2.07 (s, 3 H).

*(but-3-en-1-yloxy)(tert-butyl)diphenylsilane (**1g**).* This compound was prepared in 77% yield as a colorless oil according to the literature method.[25] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 6.4 Hz, 4 H), 7.45-7.37 (m, 6 H), 5.89-5.79 (m, 1 H), 5.08-5.01 (m, 2 H), 3.71 (t, *J* = 6.8 Hz, 2 H), 2.32 (q, *J* = 6.8 Hz, 2 H), 1.05 (s, 9 H).

*(2-methoxypent-4-en-1-yl) benzene (**1h**).* This compound was prepared in 80% yield as a colorless oil according to the literature method.[10a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2 H), 7.23-7.20 (m, 3 H), 5.91-5.80 (m, 1 H), 5.10-5.06 (m, 2 H), 3.48-3.42 (m, 1 H), 3.33 (s, 3 H), 2.83 (dd, *J* = 13.6, 6.4 Hz, 1 H), 2.74 (dd, *J* = 13.6, 6.0 Hz, 1 H), 2.31-2.18 (m, 2 H).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Procedure for screening reaction conditions and spectra of products (PDF)

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Notes

The authors declare no competing financial interest.

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