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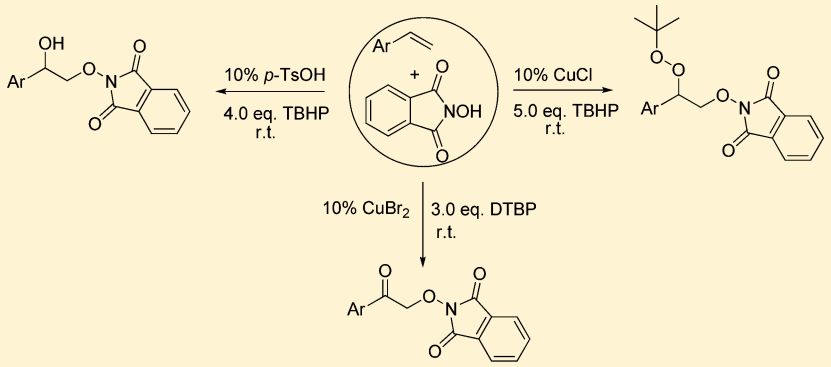
Catalyst-Controlled Dioxygenation of Olefins: An Approach to Peroxides, Alcohols, and Ketones

Xiao-Feng Xia,*[,†] Su-Li Zhu,[†] Zhen Gu,[†] Haijun Wang,[†] Wei Li,[†] Xiang Liu,[†] and Yong-Min Liang[‡]

[†]The Key Laboratory of Food Colloids and Biotechnology, Ministry of Education, School of Chemical and Material Engineering, Jiangnan University, Wuxi, Jiangsu 214122, China

[‡]State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China

Supporting Information



ABSTRACT: An efficient catalytic approach for the synthesis of substituted peroxides, alcohols, and ketones through a catalyst-controlled highly selective dioxygenation of olefins has been demonstrated. The reported methods are mild and practical, can be switched by the selection of different catalytic systems, and employ peroxide as an oxidant and a reagent at room temperature.

INTRODUCTION

Alkenes are abundant simple chemical feedstocks and organic molecules, which have an extensive application in organic synthesis, and methods for their efficient, selective functionalization are attractive to assemble more complex moleculars.[1] Among which, direct 1,2-difunctionalization of alkenes has attracted considerable attention, providing the most efficient strategy for the construction of functionalized organic compounds.[2] In recent years, a series of transition-metal-catalyzed 1,2-difunctionalizations of alkenes have been developed, such as dioxygenation,[3] oxyamidation,[4] oxyphosphorylation,[5] and diamination.[6] Dioxygenation of alkenes was the most widely used in organic synthesis, where Sharpless asymmetric dihydroxylation has been applied in the industry.[7] Despite the significance of these reactions, these kinds of 1,2-dioxygenation are still limited, and it remains challenging to control the selectivity from the same starting materials to realize different dioxygenation. Herein, we describe an efficient catalyst-controlled highly dioxygenation of alkenes for the direct synthesis of peroxides, alcohols, and ketones, which are important synthons in organic chemistry and biologically active compounds.[8]

It was known that phthalimide *N*-oxyl (PINO) radical generated from *N*-hydroxyphthalimide (NHPI) is an active catalytic species, which can realize C−H bond functionalization under the oxidizing conditions.[9] Recently, NHPI has been also utilized as a stoichiometric reactant for the construction of the C−O bond in organic synthesis.[10] Very recently, our group found that NHPI can construct the C−O bond through radical addition of alkenes, and a series of 2-azido-2-phenylethoxy-isoindolinone compounds were obtained in metal-free conditions (Scheme 1a).[11] Then, we envisaged that if oxygen radicals were instead of azide free radicals, 1,2-dioxygenation products will be generated (Scheme 1b).

RESULTS AND DISCUSSION

Our design was started by investigating the reaction of styrene **1a** with NHPI **2a** using 10% CuCl as catalyst in 1,2-dichloroethane (DCE), and a 21% **3a** was produced (Table 1, entry 1). When the loading of *t*-butylhydroperoxide (TBHP) was increased to 5.0 equiv, a 62% **3a** was obtained (entry 2). Several other copper catalysts were evaluated to increase the yield, including CuCl, CuI, CuBr, $Cu(acac)_2$, and $CuCl_2·2H_2O$, wherein CuCl displayed high catalytic activity. The solvent was also screened, such as acetonitrile, dichloromethane, ethyl acetate, acetone, toluene, dimethylformamide, and *n*-hexane, and 1,2-dichloroethane gave a better result. When the copper catalyst was omitted, no target product **3a** was obtained, but another product **4a** was separated in 60% yield. Then, when 10% *p*-toluene sulfonic acid (TsOH) was used as the catalyst, a 98% **4a** was obtained using 5.0 equiv of TBHP as oxidant in

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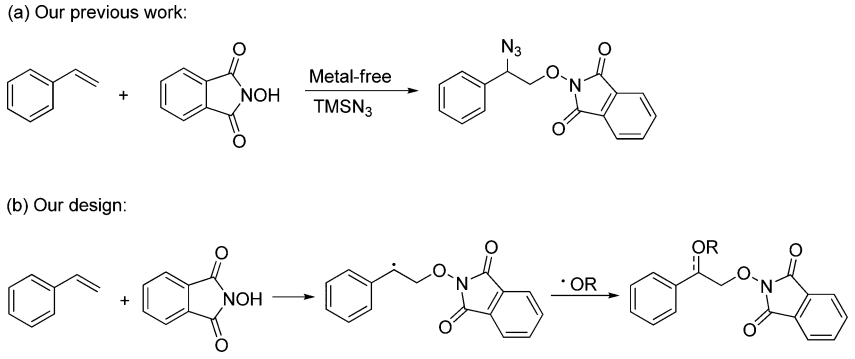
Scheme 1. Our Design



DCE (entry 21). When 4.0 equiv of TBHP was used, a similar result was obtained (entry 22). 3.0 equiv of TBHP gave a lower yield. Other acid catalysts, such as PhCOOH and HOAc, were not effective. When peroxide *tert*-butyl ether (DTBP) was used instead of TBHP, **5a** was obtained in 42% yield using 10% CuCl as catalyst. Then several copper catalysts were screened, such as $CuCl_2 \cdot 2H_2O$, $CuBr_2$, CuBr, and CuI, and $CuBr_2$ gave a better result (70% yield). Interestingly, when $CuBr_2$ was omitted, **4a** instead of **5a** was separated (77% yield).

With the optimal reaction conditions in hand, we subsequently investigated the substrate scope of this highly selective method. As we know, organic peroxides have been widely utilized in the fields of medicinal chemistry and pharmacology owing to their remarkable antimalarial, anthelmintic, and antitumor activities, such as ozonides and tetraoxanes.[12] Herein, we realized the synthesis of a new peroxide, and under the copper-catalyzed conditions, various peroxides were obtained in good to moderate yields (Scheme 2). Styrenes bearing electron-withdrawing groups such as fluoro, chloro, and bromo at the different positions performed well. α-Methylstyrene can deliver the corresponding product **3g** in moderate yield (54%). (*E*)-Prop-1-enylbenzene was also tolerated, and a mixture of diastereoisomers (**3h**, dr = 3:1) was obtained. 2-Vinylnaphthalene can afford the desired product in 44% yield (**3i**).

Furthermore, the transition-metal-free dioxygenation of alkenes was summarized in Scheme 3. A series of substituted styrenes can readily convert into the corresponding alcohols in good to excellent yields. Several useful functional groups, such as chloro, fluoro, bromo, nitro, iodo, cyano, and methyl substituents, were tolerated at the different positions of styrenes. Disappointedly, when 1-methoxy-4-vinylbenzene was used in the metal-free conditions, the reaction system was decomposed, and no target product was obtained. Moreover, (*E*)-(2-bormovinyl)benzene was also performed under the standard conditions (**4q**, dr = 3:2). Nonstyrenes such as norbornylene can also deliver the target product in good yield (**4s**, dr = 1.3:1). In addition, other alkyl alkenes such as **1t** and **1u** failed in this condition, and the starting materials can be recovered intact.

When DTBP was used as oxidant, a series of aryl ketones were obtained in moderate to good yields (Scheme 4).[13] Halo-substituted styrenes were tolerated in this transformation, forming the corresponding ketones **5c**, **5d**, and **5e** in 53%, 36%, and 40% yields, respectively. Trans-β-methylstyrene can produce the desired **5f** in 53% yield. Cyclic alkene 1,2-dihydronaphthalene can undergo the reaction to give the product **5g** in 35% yield. In all, various substituted peroxides, alcohols, and ketones can be prepared by this dioxygenation strategy in a highly chemoselective manner from the same simple olefins by selecting a different catalyst system in good to moderate yields.

In order to have an insight into the mechanism, some control experiments were performed (Scheme 5). When 2.0 equiv of 2,6-di*tert*-butyl-4-methylphenol (BHT) was added into the reaction system under the standard conditions, no desired product was detected. In addition, when 2.0 equiv of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was applied in the reaction system, no target product was separated, instead of a TEMPO-captured product **6** was obtained in 86% yield. These phenomena meant that a radical addition mechanism was involved in this transformation. The alcohol **4a** can easily convert into the ketone **5a** under the copper catalysis conditions.

Finally, the N−O bond of the product **4a** can be easily cleaved with $Mo(CO)_6$ to give 1-phenylethane-1,2-diol **7** in moderate yield (Scheme 6). According to the results of control experiments and previous report,[14] a possible reaction pathway is shown in Scheme 7. First, NHPI can easily convert into the oxygen-centered radical PINO, which then quickly added to styrene to give radical **A**. The radical intermediate **A** can be further transformed into cation intermediate **B** in the presence of peroxides, which can be attacked by water to give the product **4a**. The alcohol **4a** can be further oxidized to give the ketone **5a** under the copper catalysis conditions. One the other hand, two possible pathways generating product **3a** were proposed through nucleophilic attack of the radical intermediate **A** or carbocation intermediate **B**.

■ CONCLUSION

In summary, we have developed an efficient catalyst-controlled highly dioxygenation of olefins for the direct synthesis of substituted peroxides, alcohols, and ketones in mild reaction conditions. The products **4** can be further transformed into the diols under the reductive conditions. A radical addition process was involved in this reaction, and the radical intermediate can be captured by TEMPO. Further investigations on the mechanism and synthetic application of these reactions are ongoing in our group.

■ EXPERIMENTAL SECTION

General Remarks. Column chromatography was carried out on silica gel (200−300 grading). Unless noted ^1H NMR spectra were recorded on 400 MHz in $CDCl_3$ or *d*-acetone, ^{13}C NMR spectra were recorded on 100 MHz in $CDCl_3$ or *d*-acetone. IR spectra were recorded on an FT-IR spectrometer, and only major peaks are

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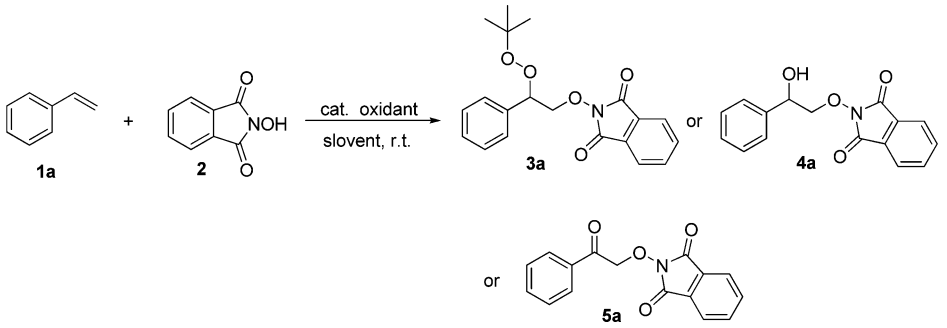
Table 1. Initial Studies for the Reaction of Dioxygenation of Alkenes[a]



entry	1a:2	catalyst	oxidant (× equiv)	solvent	yield (%)[c]
1	2:1	10% CuCl	3 equiv TBHP	DCE	21% **3a**
2	***2:1***	***10% CuCl***	***5 equiv TBHP***	***DCE***	***62% 3a*** (8%5a)
3[b]	2:1	10% CuCl	5 equiv TBHP	DCE	51% **3a**
4	2:1	10% CuCl + 10% Phen	5 equiv TBHP	DCE	49% **3a**
5	2:1	10% CuCl	5 equiv TBHP	CH_3CN	43% **3a**
6	2:1	10% CuCl	5 equiv TBHP	DMF	0
7	2:1	10% CuCl	5 equiv TBHP	DCM	36% **3a**
8	2:1	10% CuCl	5 equiv TBHP	toluene	0
9	2:1	10% CuCl	5 equiv TBHP	$CHCl_3$	0
10	2:1	10% CuCl	5 equiv TBHP	EtOAc	33% **3a**
11	2:1	10% CuCl	5 equiv TBHP	actone	30% **3a**
12	2:1	10% CuCl	5 equiv TBHP	*n*-hexane	20% **3a**
13	2:1	5% CuCl	5 equiv TBHP	DCE	58% **3a**
14	2:1	20% CuCl	5 equiv TBHP	DCE	38% **3a**
15	2:1	10% CuCl	4 equiv TBHP	DCE	43% **3a**
16	2:1	10% $CuCl_2$·2 H_2O	5 equiv TBHP	DCE	17% **3a**
17	2:1	10% CuI	5 equiv TBHP	DCE	28% **3a**
18	2:1	10% CuBr	5 equiv TBHP	DCE	47% **3a**
19	3:1	10% CuCl	5 equiv TBHP	DCE	56% **3a**
20	2:1	10% $Cu(acac)_2$	5 equiv TBHP	DCE	49% **3a**
21	*2:1*	–	*5 equiv TBHP*	*DCE*	***60% 4a***
22	***2:1***	***10% TsOH***	***5 equiv TBHP***	***DCE***	***98% 4a***
23	***2:1***	***10% TsOH***	***4 equiv TBHP***	***DCE***	***99% 4a***
24	2:1	10% TsOH	3 equiv TBHP	DCE	71% **4a**
25	2:1	10% PhCOOH	5 equiv TBHP	DCE	60% **4a**
26	2:1	10% HOAc	5 equiv TBHP	DCE	65% **4a**
27	*2:1*	*10% CuCl*	*3 equiv DTBP*	*DCE*	***42% 5a***
28	2:1	10% CuI	3 equiv DTBP	DCE	60% **5a**
29	2:1	10% CuBr	3 equiv DTBP	DCE	51% **5a**
30	2:1	10% $CuCl_2$·$2H_2O$	3 equiv DTBP	DCE	50% **5a**
31	***2:1***	***10% $CuBr_2$***	***3 equiv DTBP***	***DCE***	***70% 5a***
32	2:1	10% $CuBr_2$	3 equiv DTBP	MeCN	47% **5a**
33	*2:1*	–	*3 equiv DTBP*	*DCE*	***77% 4a***

[a]Reaction conditions: **1a** (2.0 equiv, 0.6 mmol), **2** (0.3 mmol), catalyst, oxidant, and solvent (3.0 mL), at room temperature, in air, 12 h. [b]4.0 equiv Na_2SO_4 was used. [c]Isolated yield.

reported in cm^{-1}. Melting points were determined on a microscopic apparatus and were uncorrected. All new products were further characterized by high resolution mass spectra (HRMS), high resolution mass spectrometry (HRMS) spectra was obtained on a micrOTOF-Q instrument equipped with an ESI source; copies of their ^1H NMR and ^{13}C NMR spectra are provided. Commercially available reagents **1**, **2**, and solvents were used without further purification.

Typical Procedure for the Synthesis of Products 3. To a 20 mL Schlenk tube was added *N*-hydroxyphthalimide (**2**, 0.3 mmol, 48.9 mg), styrene (**1**, 0.6 mmol), 10% CuCl (0.03 mmol), TBHP (5.0 equiv, 1.5 mmol, 5−6 M in decane), and DCE (3.0 mL). The reaction mixture was then stirred for 12 h at room temperature in air. When the reaction was finished, the resulting mixture was quenched with water (10 mL) and extracted twice with EtOAc (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated. Purification of the crude product by flash column chromatography afforded the product **3** (petroleum ether/ethyl acetate as eluent (20:1)).

*2-(2-(tert-Butylperoxy)-2-phenylethoxy)isoindoline-1,3-dione (**3a**).* White solid, mp = 73−74 °C, yield: 66 mg, 62%. ^1H NMR (400 M H_Z, $CDCl_3$): 7.80−7.83 (m, 2 H), 7.72−7.74 (m, 2 H), 7.42−7.45 (m, 2 H), 7.29−7.37 (m, 3 H), 5.36−5.39 (m, 1 H), 4.60−4.64 (m, 1 H), 4.42−4.46 (m, 1 H), 1.18 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.0, 136.8, 134.3, 128.3, 127.3, 123.3, 83.3, 80.6, 78.4, 53.4, 26.2; HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{21}NO_5Na$: M + Na = 378.1317; found: 378.1320. IR (cm^{-1}): 1791, 1734, 1188, 1018, 877, 699.

*2-(2-(tert-Butylperoxy)-2-p-tolylethoxy)isoindoline-1,3-dione (**3b**).* Oil, yield: 78.6 mg, 71%. ^1H NMR (400 M H_Z, $CDCl_3$): 7.70−

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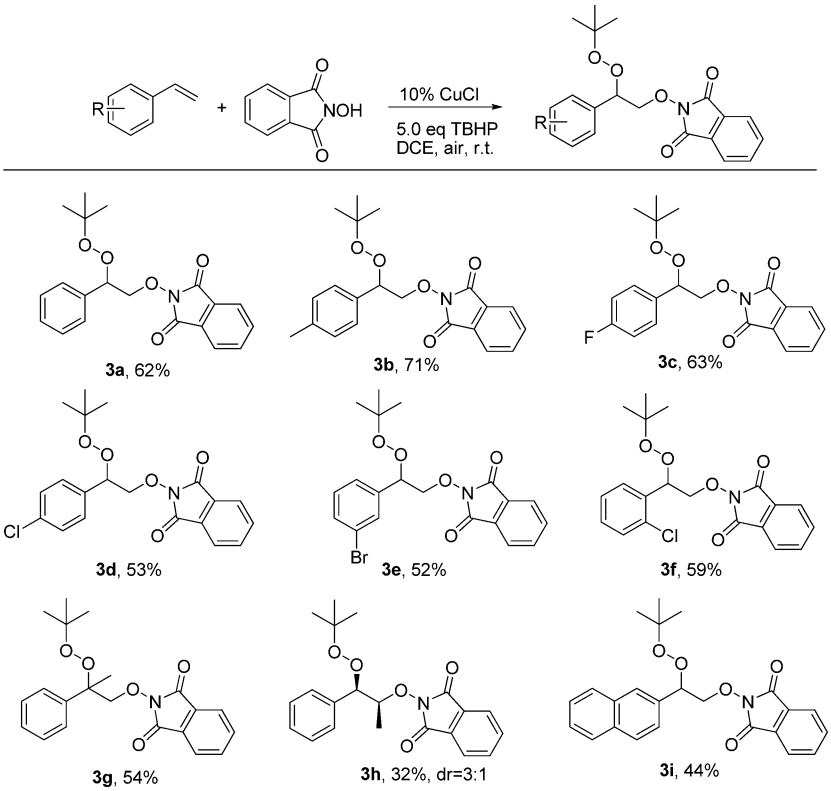
Scheme 2. Cu-Catalyzed Selective Synthesis of Peroxides 3[a]



[a]For reaction conditions, see Table 1, entry 2. Yields shown are of isolated products. dr determined by ^{1}H NMR spectroscopy.

7.72 (m, 2 H), 7.61−7.63 (m, 2 H), 7.22−7.24 (m, 2 H), 7.04−7.06 (m, 2 H), 5.23−5.26 (m, 1 H), 4.51−4.55 (m, 1 H), 4.33−4.37 (m, 1 H), 2.21 (s, 3 H), 1.09 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.1, 138.1, 133.8, 127.4, 123.3, 83.1, 80.6, 78.4, 26.2, 21.1; HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{23}NO_5Na$: M + Na = 392.1474; found: 392.1468. IR (cm^{-1}): 2978, 2927, 1790, 1732, 1515, 1468, 1363, 1188, 1131, 1018, 998, 877, 814, 701.

*2-(2-(tert-Butylperoxy)-2-(4-fluorophenyl)ethoxy)isoindoline-1,3-dione (**3c**).* Mp = 77−78 °C, yield: 70.5 mg, 63%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.73−7.82 (m, 4 H), 7.42−7.44 (m, 2 H), 7.02−7.06 (m, 2 H), 5.34−5.37 (m, 1 H), 4.58−4.63 (m, 1 H), 4.40−4.44 (m, 1 H), 1.18 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.1, 134.4, 129.3, 129.2, 128.8, 123.4, 115.3, 115.1, 82.5, 80.8, 78.3, 26.2; HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{20}NFO_5Na$: M + Na = 396.1223; found: 396.1228. IR (cm^{-1}): 3438, 1791, 1732, 1511, 1364, 1188, 1082, 1018, 877, 701.

*2-(2-(tert-Butylperoxy)-2-(4-chlorophenyl)ethoxy)isoindoline-1,3-dione (**3d**).* Mp = 65−66 °C, yield: 61.9 mg, 53%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.73−7.81 (m, 4 H), 7.38−7.40 (m, 2 H), 7.31−7.34 (m, 2 H), 5.33−5.36 (m, 1 H), 4.56−4.60 (m, 1 H), 4.38−4.42 (m, 1 H), 1.18 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.1, 135.5, 134.4, 134.2, 128.8, 128.5, 123.4, 82.5, 80.9, 78.2, 26.2; HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{20}NClO_5Na$: M + Na = 412.0928; found: 412.0922. IR (cm^{-1}): 3070, 2978, 1790, 1732, 1485, 1468, 1363, 1188, 1018, 998, 877, 814, 701.

*2-(2-(3-Bromophenyl)-2-(tert-butylperoxy)ethoxy)isoindoline-1,3-dione (**3e**).* Oil, yield: 67.5 mg, 52%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.81−7.83 (m, 2 H), 7.73−7.75 (m, 2 H), 7.59 (s, 1 H), 7.38 (m, 2 H), 7.21−7.24 (m, 1 H), 5.34−5.36 (m, 1 H), 4.53−4.58 (m, 1 H), 4.37−4.40 (m, 1 H), 1.20 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.1, 139.3, 134.4, 130.4, 128.8, 125.9, 123.4, 122.4, 82.6, 80.9, 78.3, 26.2; HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{20}NBrO_5Na$: M + Na = 456.0423; found: 456.0417. IR (cm^{-1}): 1791, 1731, 1468, 1364, 1188, 1131, 1081, 1019, 999, 877, 785, 700.

*2-(2-(tert-Butylperoxy)-2-(2-chlorophenyl)ethoxy)isoindoline-1,3-dione (**3f**).* Oil, yield: 68.9 mg, 59%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.73−7.84 (m, 4 H), 7.60−7.62 (m, 1 H), 7.24−7.33 (m, 3 H), 5.84−5.86 (m, 1 H), 4.42−4.43 (m, 2 H), 1.25 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.0, 134.5, 134.4, 132.6, 129.4, 126.8, 123.4, 81.0, 80.5, 77.8, 26.3; HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{20}NClO_5Na$: M + Na = 412.0928; found: 412.0922. IR (cm^{-1}): 1791, 1732, 1468, 1364, 1188, 1133, 757, 701.

*2-(2-(tert-Butylperoxy)-2-phenylpropoxy)isoindoline-1,3-dione (**3g**).* Oil, yield: 59.8 mg, 54%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.78−7.80 (m, 2 H), 7.69−7.72 (m, 2 H), 7.59−7.61 (m, 2 H), 7.34−7.37 (m, 2 H), 7.26−7.28 (m, 1 H), 4.61 (s, 2 H), 1.81 (s, 3 H), 1.20 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.0, 141.5, 134.2, 127.9, 127.5, 126.2, 123.2, 82.3, 80.7, 79.5, 26.4, 21.9; HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{23}NO_5Na$: M + Na = 392.1474; found: 392.1468. IR (cm^{-1}): 1791, 1732, 1468, 1364, 1188, 1129, 1019, 1000, 877, 762, 699.

*2-(1-(tert-Butylperoxy)-1-phenylpropan-2-yloxy)isoindoline-1,3-dione (**3h**).* Oil, dr = 3:1, yield: 35.4 mg, 32%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.71−7.85 (m, 4 H), 7.52−7.54 (m, 2 H), 7.34−7.37 (m, 3 H), 7.28−7.30 (m, 1 H), 5.25−5.27 (m, 0.3 H), 5.20−5.21 (m, 1 H), 4.75−4.80 (m, 1 H), 1.36 (*d*, *J* = 8.0 Hz, 3 H), 1.19 (s, 9 H), 1.13 (*d*, *J* = 4.0 Hz, 1 H), 1.07 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 137.1, 134.3, 127.9, 127.8, 123.3, 86.8, 86.6, 85.0, 84.0, 80.5, 26.3, 26.2, 14.1; HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{23}NO_5Na$: M + Na = 392.1474; found: 392.1468. IR (cm^{-1}): 1791, 1737, 1381, 1364, 1189, 977, 878, 700.

*2-(2-(tert-Butylperoxy)-2-(naphthalene-2-yl)ethoxy)isoindoline-1,3-dione (**3i**).* Oil, yield: 53.5 mg, 44%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.92 (s, 1 H), 7.75−7.88 (m, 5 H), 7.65−7.67 (m, 2 H), 7.52−7.54 (m, 1 H), 7.44−7.46 (m, 2 H), 5.54−5.57 (m, 1 H), 4.68−4.72 (m, 1 H), 4.51−4.54 (m, 1 H), 1.21 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.1, 134.4, 134.3, 133.3, 133.1, 128.8, 128.1, 127.6, 126.9, 126.1, 124.9, 1123.3, 83.5, 80.8, 78.4, 26.3; HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{23}NO_5Na$: M + Na = 428.1474; found: 428.1468. IR (cm^{-1}): 1790, 1732, 1364, 1188, 1128, 1018, 877, 700.

Typical Procedure for the Synthesis of Products 4. To a 20 mL Schlenk tube was added *N*-hydroxyphthalimide (**2**, 0.3 mmol, 48.9 mg), styrene (**1**, 0.6 mmol), 10% $TsOH{\cdot}H_2O$ (0.03 mmol), TBHP (4.0 equiv, 1.2 mmol, 5−6 M in decane), and DCE (3.0 mL). The

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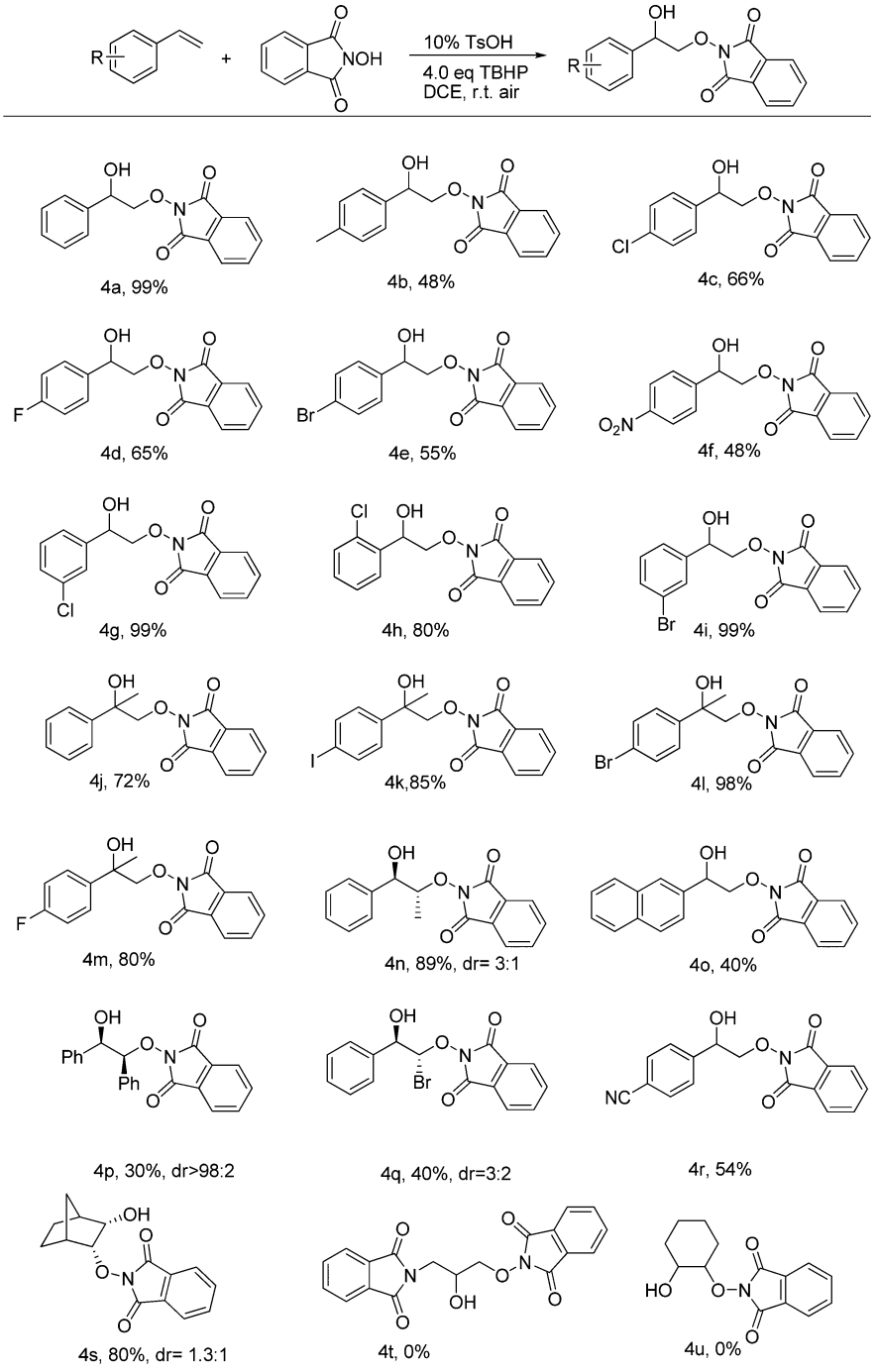
Scheme 3. Transition-Metal-Free Selective Synthesis of Alcohols 4[a]



[a]For reaction conditions, see Table 1, entry 23. Yields shown are of isolated products. dr determined by ^{1}H NMR spectroscopy.

reaction mixture was then stirred for 12 h at room temperature in air. After the reaction was finished, the resulting mixture was quenched with water (10 mL) and extracted twice with EtOAc (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated. Purification of the crude product by flash column chromatography afforded the product **4** (petroleum ether/ethyl acetate as eluent (3:1)).

*2-(2-Hydroxy-2-phenylethoxy)isoindoline-1,3-dione (**4a**).* Oil, yield: 84 mg, 99%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.73 (s, 1 H), 7.82−7.86 (m, 2 H), 7.75−7.78 (m, 2 H), 7.32−7.39 (m, 5 H), 5.42 (m, 1 H), 4.50 (d, J = 4.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 135.7, 134.7, 128.6, 128.5, 127.0, 123.7, 85.3, 78.7; HRMS (ESI) m/z: calcd for $C_{16}H_{13}NO_4Na$: M + Na = 306.0742; found: 306.0722. IR (cm^{-1}): 3393, 1788, 1730, 1187, 1019, 997, 878, 699.

*2-(2-Hydroxy-2-p-tolylethoxy)isoindoline-1,3-dione (**4b**).* Mp = 164−166 °C, yield: 42.8 mg, 48%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.58 (s, 1 H), 7.75−7.85 (m, 4 H), 7.26−7.29 (m, 2 H), 7.16−7.18 (m, 2 H), 5.36−5.39 (m, 1 H), 4.49−4.50 (m, 2 H), 2.33 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.0, 145.1, 134.8, 134.6, 134.3, 129.3, 128.4, 126.1, 123.9, 123.6, 115.0, 83.6, 78.4, 21.8; HRMS (ESI) m/z: calcd for $C_{17}H_{15}NO_4Na$: M + Na = 320.0899; found: 320.0883. IR (cm^{-1}): 3397, 1790, 1732, 1186, 877, 702.

*2-(2-(4-Chlorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione (**4c**).* Mp = 83−84 °C, yield: 62.8 mg, 66%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.81 (s, 1 H), 7.77−7.86 (m, 4 H), 7.29−7.39 (m, 4 H),

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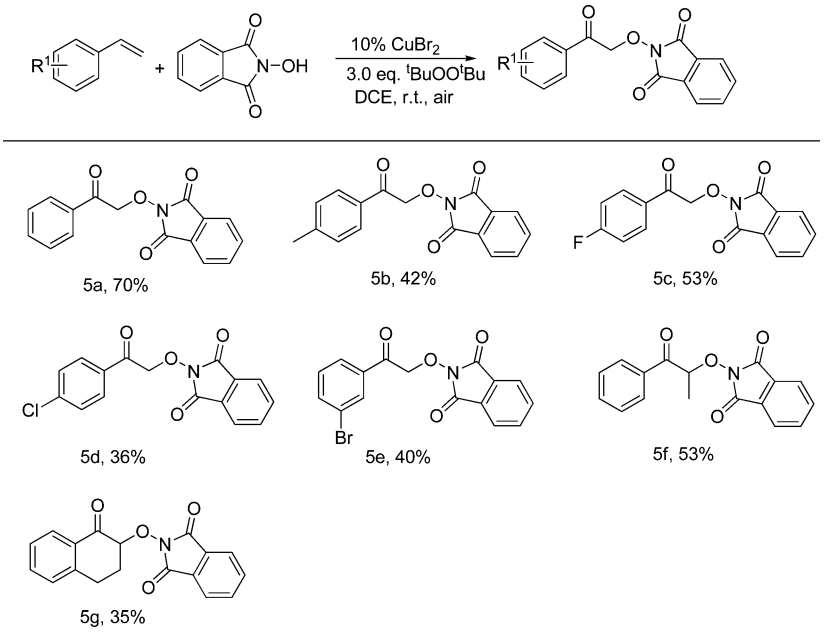
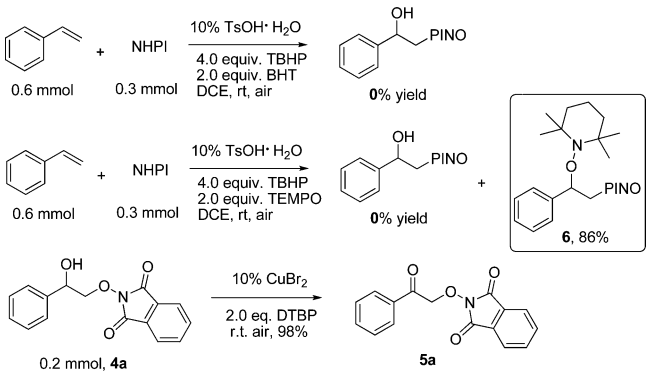
Scheme 4. Cu-Catalyzed Selective Synthesis of Aryl Ketones 5[a]

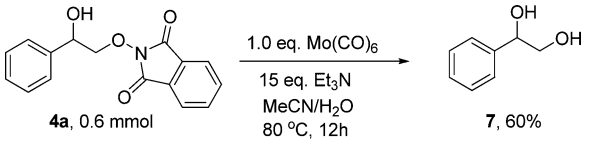


[a]For reaction conditions, see Table 1, entry 31. Yields shown are of isolated products.

Scheme 5. Mechanistic Experiments



Scheme 6. Transformation of the Product 4a



5.38–5.41 (m, 1 H), 4.48–4.50 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 134.8, 128.9, 128.6, 128.5, 123.8, 84.6, 78.5; HRMS (ESI) *m/z*: calcd for $C_{16}H_{12}NClO_4Na$: M + Na = 340.0353; found: 340.0343. IR (cm^{-1}): 3372, 1789, 1731, 1187, 1133, 1090, 1015, 997, 878, 702.

2-(2-(4-Fluorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione ***(4d)***. Mp = 106–107 °C, yield: 58.7 mg, 65%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.82 (s, 1 H), 7.75–7.85 (m, 4 H), 7.38–7.40 (m, 2 H), 7.02–7.06 (m, 2 H), 5.36–5.39 (m, 1 H), 4.48 (d, J = 4.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.8, 134.8, 134.7, 128.9, 128.6, 123.8, 123.7, 115.8, 115.6, 84.6, 78.6; HRMS (ESI) *m/z*: calcd for $C_{16}H_{12}NFO_4Na$: M + Na = 324.0648; found: 324.0648. IR (cm^{-1}): 3371, 1790, 1732, 1600, 1510, 1231, 878, 838, 701.

2-(2-(4-Bromophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione ***(4e)***. Mp = 87–89 °C, yield: 59.6 mg, 55%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.78 (s, 1 H), 7.76–7.85 (m, 4 H), 7.48–7.50 (m, 2 H), 7.28–7.30 (m, 2 H), 5.35–5.38 (m, 1 H), 4.43–4.50 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 134.8, 131.8, 128.8, 128.6, 123.8, 84.6, 78.4; HRMS (ESI) *m/z*: calcd for $C_{16}H_{12}NBrO_4Na$: M + Na = 383.9847; found: 383.9813. IR (cm^{-1}): 3363, 1789, 1731, 1187, 1081, 1071, 878, 701.

2-(2-Hydroxy-2-(4-nitrophenyl)ethoxy)isoindoline-1,3-dione ***(4f)***. Mp = 119–120 °C, yield: 47 mg, 48%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 8.23–8.27 (m, 2 H), 7.77–7.88 (m, 4 H), 7.63–7.65 (m, 2 H), 5.50–5.52 (m, 1 H), 4.46–4.57 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 148.1, 143.0, 134.9, 134.8, 134.3, 128.6, 127.0, 124.0, 123.9, 123.8, 123.7, 123.6, 84.3, 78.0; HRMS (ESI) *m/z*: calcd for $C_{16}H_{12}N_2O_6Na$: M + Na = 351.0593; found: 351.0588. IR (cm^{-1}): 3325, 1790, 1731, 1520, 1348, 1187, 878, 855, 701.

2-(2-(3-Chlorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione ***(4g)***. Mp = 100–101 °C, yield: 94 mg, 99%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.78 (s, 1 H, OH), 7.77–7.87 (m, 4 H), 7.42 (s, 1 H), 7.30 (m, 3 H), 5.37–5.40 (m, 1 H), 4.46–4.48 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 137.8, 134.6, 129.9, 128.9, 128.8, 128.6, 127.2, 125.2, 123.8, 84.7, 78.4; HRMS (ESI) *m/z*: calcd for $C_{16}H_{12}NClO_4Na$: M + Na = 340.0353; found: 340.0347. IR (cm^{-1}): 3365, 1790, 1731, 1375, 1187, 1081, 1019, 998, 877, 787, 701.

2-(2-(2-Chlorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione ***(4h)***. Mp = 96–97 °C, yield:76.1 mg, 80%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.96 (s, 1 H), 7.78–7.88 (m, 4 H), 7.58 (m, 1 H), 7.26–7.35 (m, 3 H), 5.84–5.87 (m, 1 H), 4.50–4.53 (m, 1 H), 4.27–4.32 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.8, 134.7, 129.6, 127.9, 127.1, 123.8, 83.0, 77.7; HRMS (ESI) *m/z*: calcd for $C_{16}H_{12}NClO_4Na$: M + Na = 340.0353; found: 340.0348. IR (cm^{-1}): 3393, 1789, 1731, 1187, 1019, 878, 759.

2-(2-(3-Bromophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione ***(4i)***. Mp = 127–128 °C, yield:107 mg, 99%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.64 (s, 1 H), 7.78–7.86 (m, 4 H), 7.46–7.58 (m, 2 H), 7.25–7.34 (m, 2 H), 5.38 (m, 1 H), 4.48 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 138.1, 134.8, 130.3, 128.6, 125.7, 123.8, 122.8, 84.7, 78.5; HRMS (ESI) *m/z*: calcd for $C_{16}H_{12}NBrO_4Na$: M + Na = 383.9847; found: 383.9842. IR (cm^{-1}): 3395, 1784, 1725, 1465, 1363, 1187, 1125, 877, 785, 695.

2-(2-Hydroxy-2-phenylpropoxy)isoindoline-1,3-dione ***(4j)***. Mp = 107–108 °C, yield: 64.1 mg, 72%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 9.87 (s, 1 H), 7.78–7.87 (m, 4 H), 7.52–7.54 (m, 2 H), 7.32–7.42 (m, 3 H), 4.65–4.72 (m, 2 H), 1.69 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.8, 140.7, 134.8, 128.5, 127.9, 125.3, 123.8, 84.4, 79.7, 22.9; HRMS

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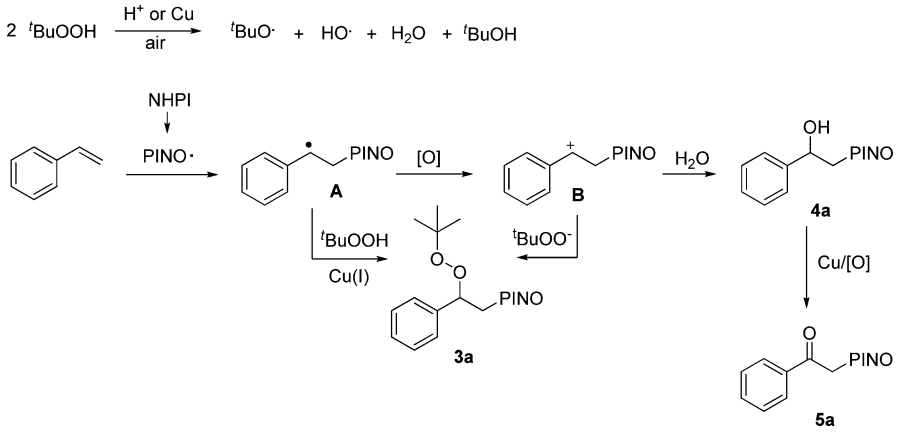
Scheme 7. A Possible Reaction Mechanism



(ESI) *m/z*: calcd for $C_{17}H_{15}NO_4Na$: M + Na = 320.0899; found: 320.0898. IR (cm^{-1}): 3371, 1788, 1728, 1188, 1020, 878, 699.

2-(2-Hydroxy-2-(4-iodophenyl)propoxy)isoindoline-1,3-dione (***4k***). Mp = 80−81 °C, yield: 107.8 mg, 85%. ^1H NMR (400 M H_Z, $CDCl_3$): 10.00 (s, 1 H, OH), 7.76−7.85 (m, 4 H), 7.67−7.70 (m, 2 H), 7.25−7.26 (m, 2 H), 4.58−4.66 (m, 2 H), 1.62 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 140.4, 137.4, 134.8, 128.4, 127.4, 123.7, 93.6, 84.0, 79.3, 22.6; HRMS (ESI) *m/z*: calcd for $C_{17}H_{14}INO_4Na$: M + Na = 445.9865; found: 445.9860. IR (cm^{-1}): 3374, 1789, 1737, 1486, 1467, 1188, 1004, 878, 820, 785.

2-(2-(4-Bromophenyl)-2-hydroxypropoxy)isoindoline-1,3-dione (***4l***). Mp = 101−102 °C, yield: 110 mg, 98%. ^1H NMR (400 M H_Z, $CDCl_3$): 9.91 (s, 1 H, OH), 7.74−7.83 (m, 4 H), 7.45−7.48 (m, 2 H), 7.36−7.39 (m, 2 H), 4.57−4.65 (m, 2 H), 1.62 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 139.7, 134.8, 131.4, 127.2, 123.7, 121.8, 83.9, 79.4, 22.6; HRMS (ESI) *m/z*: calcd for $C_{17}H_{14}NBrO_4Na$: M + Na = 398.0004; found: 397.9998. IR (cm^{-1}): 3373, 1788, 1731, 1488, 1467, 1392, 1188, 1133, 1021, 878, 824, 702.

2-(2-(4-Fluorophenyl)-2-hydroxypropoxy)isoindoline-1,3-dione (***4m***). Oil, yield: 75.6 mg, 80%. ^1H NMR (400 M H_Z, $CDCl_3$): 9.92 (s, 1 H), 7.76−7.86 (m, 4 H), 7.48−7.51 (m, 2 H), 7.03−7.07 (m, 2 H), 4.60−4.67 (m, 2 H), 1.64 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 134.8, 127.4, 127.3, 123.8, 115.3, 115.1, 83.9, 79.6, 22.7; HRMS (ESI) *m/z*: calcd for $C_{17}H_{14}NFO_4Na$: M + Na = 338.0805; found: 338.0799. IR (cm^{-1}): 3376, 1789, 1731, 1605, 1511, 1232, 1188, 1021, 1102, 878, 837, 701.

2-(1-Hydroxy-1-phenylpropan-2-yloxy)isoindoline-1,3-dione (***4n***). Mp = 57−59 °C, dr = 3:1, yield: 79.3 mg, 89%. ^1H NMR (400 M H_Z, $CDCl_3$): 10.1 (s, 1 H, OH), 7.83−7.86 (m, 2.5 H), 7.75−7.77 (m, 2.6 H), 7.43−7.44 (m, 2 H), 7.32−7.38 (m, 4 H), 5.28 (s, 0.5 H), 5.16−5.17 (m, 1 H), 5.11−5.13 (m, 0.32 H), 4.76−4.82 (m, 1 H), 4.61−4.65 (m, 0.34 H), 1.67−1.68 (d, J = 4.0 Hz, 0.47 H), 1.27−1.29 (m, 3 H), 1.18−1.19 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 164.5, 134.9, 134.7, 134.6, 128.6, 127.7, 123.7, 123.6, 90.7, 87.9, 85.5, 84.4, 16.7, 13.9; HRMS (ESI) *m/z*: calcd for $C_{17}H_{15}NO_4Na$: M + Na = 320.0899; found: 320.0897. IR(cm^{-1}): 3376, 1790, 1738, 1378, 1188, 978, 878, 700.

2-(2-Hydroxy-2-(naphthalene-2-yl)ethoxy)isoindoline-1,3-dione (***4o***). Oil, yield: 40 mg, 40%. ^1H NMR (400 M H_Z, $CDCl_3$): 7.90 (s, 1 H), 7.80−7.85 (m, 5 H), 7.73−7.75 (m, 2 H), 7.47−7.51 (m, 3 H), 5.59−5.61 (m, 1 H), 4.60−4.61 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 134.7, 133.3, 133.2, 133.1, 128.6, 128.5, 128.1, 127.6, 126.6, 126.4, 126.3, 124.4, 123.7, 85.5, 78.8; HRMS (ESI) *m/z*: calcd for $C_{20}H_{15}NO_4Na$: M + Na = 356.0899; found: 356.0893. IR(cm^{-1}): 3430, 1790, 1731, 1374, 1187, 877, 701.

2-(2-Hydroxy-1,2-diphenylethoxy)isoindoline-1,3-dione (***4p***). Mp = 130−131 °C, dr > 98:2, yield: 32.3 mg, 30%. ^1H NMR (400 M H_Z, $CDCl_3$): 10.28 (s, 1 H, OH), 7.73−7.80 (m, 4 H), 7.21−7.33 (m, 10 H), 5.93 (*d*, *J* = 4.0 Hz, 1 H), 5.27 (*d*, *J* = 4.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 164.0, 134.7, 133.9, 128.8, 127.7, 123.6, 89.1, 87.9; HRMS (ESI) *m/z*: calcd for $C_{22}H_{17}NO_4Na$: M + Na = 382.1055; found: 382.1050. IR (cm^{-1}): 3373, 1790, 1731, 1375, 1188, 978, 877, 699.

2-(1-Bromo-2-hydroxy-2-phenylethoxy)isoindoline-1,3-dione (***4q***). Oil, dr = 3:2, yield: 43.3 mg, 40%. ^1H NMR (400 M H_Z, $CDCl_3$): 10.0 (s, 1 H, OH), 8.24−8.26 (m, 1 H), 7.81−7.88 (m, 7 H), 7.35−7.39 (m, 7 H), 6.70−6.72 (m, 0.4 H), 6.52 (s, 0.3 H), 6.34−6.36 (m, 0.6 H), 5.45−5.47 (m, 0.4 H), 5.27 (m, 0.4 H), 5.08−5.10 (m, 0.6 H); ^{13}C NMR (100 MHz, $CDCl_3$): 186.3, 163.6, 162.9, 162.5, 162.3, 137.5, 135.1, 134.5, 128.8, 128.4, 126.8, 124.2, 124.1, 123.9, 97.2, 94.6, 91.6, 87.8, 85.4, 74.7; HRMS (ESI) *m/z*: calcd for $C_{16}H_{12}NBrO_4Na$: M + Na =383.9847; found: 383.9842. IR (cm^{-1}): 3396, 1740, 1451, 761, 698.

4-(2-(1,3-Dioxoisoindolin-2-yloxy)-1-hydroxyethyl)benzonitrile (***4r***). White solid, mp = 109−110 °C, yield: 50 mg, 54%. ^1H NMR (400 M H_Z, $CDCl_3$): 7.84−7.87 (m, 2 H), 7.78−7.81 (m, 2 H), 7.67 (d, *J* = 8.0 Hz, 2 H), 7.57 (d, *J* = 8.0 Hz, 2 H), 6.39 (s, 1 H, OH), 5.44−5.47 (m, 1 H), 4.48−4.50 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.6, 141.2, 134.8, 132.3, 128.5, 126.8, 123.8, 118.3, 112.5, 84.4, 77.9; IR (cm^{-1}): 2228, 1786, 1702, 1375, 1263, 1185, 1063, 876, 792; HRMS (ESI) *m/z*: calcd for $C_{17}H_{12}N_2NaO_4$: M + Na = 331.0695; found: 331.0685.

4s. Major: 2-((*cis*)-3-Hydroxybicyclo[2.2.1]heptan-2-yloxy)-isoindoline-1,3-dione. Mp = 148−149 °C, dr = 1.3:1, yield: 65.5 mg, 80%. ^1H NMR (400 M H_Z, $CDCl_3$): 10.6 (s, 1 H, OH), 7.80−7.87 (m, 4 H), 4.36 (d, *J* = 5.2 Hz, 1 H), 4.14 (d, *J* = 4.8 Hz, 1 H), 2.94 (s, 1 H), 2.31 (s, 1 H), 2.03−2.05 (m, 1 H), 1.53−1.59 (m, 2 H), 1.17−1.25 (m, 2 H), 0.99−1.03 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 164.3, 134.8, 128.6, 123.8, 93.4, 88.9, 41.7, 39.8, 33.5, 25.9, 22.9; HRMS (ESI) *m/z*: calcd for $C_{15}H_{15}NO_4Na$: M + Na = 296.0899; found: 296.0893. IR (cm^{-1}): 3383, 2854, 2876, 1789, 1731, 1467, 1378, 1188, 1016, 993, 964, 878, 702. Minor: 2-((*trans*)-3-Hydroxybicyclo[2.2.1]-heptan-2-yloxy)isoindoline-1,3-dione. Mp = 60−62 °C. ^1H NMR (400 M H_Z, $CDCl_3$): 8.83 (s, 1 H, OH), 7.72−7.82 (m, 4 H), 4.59 (t, *J* = 1.2 Hz, 1 H), 4.19 (s, 1 H), 2.63 (s, 1 H), 2.54 (d, *J* = 3.6 Hz, 1 H), 2.02−2.04 (m, 1 H), 1.56−1.65 (m, 2 H), 1.22−1.33 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 164.1, 134.4, 128.8, 123.5, 92.9, 90.7, 41.1, 39.5, 34.4, 24.7, 19.8; HRMS (ESI) *m/z*: calcd for $C_{15}H_{15}NO_4Na$: M + Na = 296.0899; found: 296.0893.

Typical Procedure for the Synthesis of Products 5. To a 20 mL Schlenk tube was added *N*-hydroxyphthalimide (**2**, 0.3 mmol, 48.9 mg), styrene (**1**, 0.6 mmol), 10% $CuBr_2$ (0.03 mmol), DTBP (3.0 equiv, 0.9 mmol), and DCE (3.0 mL). The reaction mixture was then stirred for 12 h at room temperature in air. After the reaction, the resulting mixture was quenched with water (10 mL) and extracted twice with EtOAc (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated. Purification of the crude product by flash column chromatography afforded the product **5** (petroleum ether/ethyl acetate as eluent (3:1)).

2-(2-oxo-2-Phenylethoxy)isoindoline-1,3-dione (***5a***). Mp = 108−109 °C, yield: 59 mg, 70%. ^1H NMR (400 M H_Z, $CDCl_3$): 7.98−7.99

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(m, 2 H), 7.75−7.83 (m, 4 H), 7.60 (m, 1 H), 7.48 (m, 2 H), 5.46 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 192.1, 162.9, 134.8, 134.6, 133.9, 128.7, 128.6, 128.4, 128.1, 126.1, 123.7, 123.6, 78.3; HRMS (ESI) *m/z*: calcd for $C_{16}H_{11}NO_4Na$: M + Na = 304.0586; found: 304.0580. IR (cm^{-1}): 3062, 2937, 1790, 1731, 1373, 1187, 1081, 877, 700.

*2-(2-oxo-2-p-Tolylethoxy)isoindoline-1,3-dione (**5b**).* Mp = 147−149 °C, yield: 37.2 mg, 42%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.83−7.90 (m, 4 H), 7.74−7.77 (m, 2 H), 7.27−7.28 (m, 2 H), 5.42 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.8, 162.9, 145.0, 134.8, 134.6, 129.1, 128.4, 126.1, 123.8, 123.6, 78.4, 21.7; HRMS (ESI) *m/z*: calcd for $C_{17}H_{13}NO_4Na$: M + Na = 318.0742; found: 318.0737. IR (cm^{-1}): 1787, 1730, 1606, 1371, 1185, 1130, 983, 876, 814, 701.

*2-(2-(4-Fluorophenyl)-2-oxoethoxy)isoindoline-1,3-dione (**5c**).* Mp = 138−140 °C, yield: 47.7 mg, 53%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 8.17−8.21 (m, 2 H), 7.83−7.89 (m, 4 H), 7.31−7.35 (m, 2 H), 5.53 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 190.8, 162.6, 134.7, 134.6, 134.3, 131.4, 128.3, 123.2, 122.8, 115.8, 115.6, 114.9, 114.7, 78.7; HRMS (ESI) *m/z*: calcd for $C_{16}H_{10}NFO_4Na$: M + Na = 322.0492; found: 322.0486. IR (cm^{-1}): 1790, 1732, 1599, 1509, 1231, 1187, 877, 838, 701.

*2-(2-(4-Chlorophenyl)-2-oxoethoxy)isoindoline-1,3-dione (**5d**).* Mp = 107−108 °C, yield: 34 mg, 36%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.98−8.00 (m, 2 H), 7.76−7.83 (m, 4 H), 7.74−7.79 (m, 2 H), 5.38 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.2, 162.9, 140.6, 134.7, 132.7, 129.1, 128.7, 123.7, 78.6; HRMS (ESI) *m/z*: calcd for $C_{16}H_{10}NClO_4Na$: M + Na = 338.0196; found: 338.0191. IR (cm^{-1}): 1790, 1732, 1374, 1091, 991, 701.

*2-(2-(3-Bromophenyl)-2-oxoethoxy)isoindoline-1,3-dione (**5e**).* Mp = 96−97 °C, yield: 43.2 mg, 40%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 8.15−8.16 (m, 1 H), 7.95−7.97 (m, 1 H), 7.76−7.85 (m, 4 H), 7.56 (s, 1 H), 7.39−7.42 (m, 1 H), 5.39 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.1, 162.9, 136.9, 134.9, 134.8, 134.7, 131.4, 127.0, 123.9, 123.8, 123.7, 123.1, 78.5; HRMS (ESI) *m/z*: calcd for $C_{16}H_{11}NBrO_4$: M + H= 359.9871; found: 359.9866. IR (cm^{-1}): 1790, 1732, 1468, 1374, 1187, 995, 877, 786.

*2-(1-oxo-1-Phenylpropan-2-yloxy)isoindoline-1,3-dione (**5f**).*[13] White solid; mp =178−179 °C, yield: 47 mg, 53%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 8.15−8.17 (m, 2 H), 7.81−7.84 (m, 2 H), 7.74−7.76 (m, 2 H), 7.58−7.62 (m, 1 H), 7.48−7.51 (m, 2 H), 5.73−5.78 (m, 1 H), 1.69 (d, *J* = 8.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 195.3, 163.6, 134.6, 134.2, 133.6, 128.6, 123.6, 123.5, 83.6, 16.1; IR (cm^{-1}): 1790, 1735, 1679, 1595, 1451, 1374, 1232, 1188, 1129, 1036, 977, 877.

*2-(1-oxo-1,2,3,4-Tetrahydronaphthalen-2-yloxy)isoindoline-1,3-dione (**5g**).*[13] Yellow solid; mp=171−172 °C, yield: 32 mg, 35%. ^{1}H NMR (400 M H_Z, $CDCl_3$): 8.04 (d, *J* = 8.0 Hz, 1 H), 7.82−7.84 (m, 2 H), 7.74−7.76 (m, 2 H), 7.53 (t, *J* = 8.0 Hz, 1 H), 7.35 (t, *J* = 8.0 Hz, 1 H), 7.28 (d, *J* = 8.0 Hz, 1 H), 4.94−4.97 (m, 1 H), 3.31−3.38 (m, 1 H), 2.96−2.99 (m, 1 H), 2.53−2.61 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 192.2, 163.2, 143.2, 134.8, 134.4, 131.2, 128.8, 128.6, 127.9, 127.4, 123.8, 123.6, 84.3, 28.2, 25.7; IR (cm^{-1}): 1790, 1734, 1679, 1597, 1454, 1352, 1295, 1241, 1184, 1152, 1063, 1025, 978, 878.

The Procedure for the Synthesis of Product 6. To a 20 mL Schlenk tube was added *N*-hydroxyphthalimide (**2**, 0.3 mmol, 48.9 mg), styrene (**1**, 0.6 mmol, 62.4 mg), 10% TsOH·H_2O (0.03 mmol, 5.7 mg), TBHP (4.0 equiv, 1.2 mmol, 5−6 M in decane), TEMPO (2.0 equiv, 0.6 mmol, 93.6 mg), and DCE (3.0 mL). The reaction mixture was then stirred for 12 h at room temperature in air. After the reaction, the resulting mixture was quenched with water (10 mL) and extracted twice with EtOAc (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated. Purification of the crude product by flash column chromatography afforded the product **6** (petroleum ether/ethyl acetate as eluent (10:1)).

*2-(2-Phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)ethoxy)-isoindolin-1,3-dione(**6**).* Oil ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.67−7.77 (m, 4 H), 7.46−7.47 (m, 2 H), 7.33−7.35 (m, 2 H), 7.25−7.31 (m, 1 H), 5.13−5.16 (m, 1 H), 4.73−4.75 (m, 1 H), 4.48−4.52 (m, 2 H), 1.20−1.46 (m, 13 H), 1.05 (m, 3 H), 0.72 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.0, 140.0, 134.2, 128.3, 127.7, 123.2, 83.2, 80.1, 60.0, 40.3, 33.9, 20.2, 17.0; HRMS (ESI) *m/z*: calcd for $C_{25}H_{30}N_2O_4Na$: M + H = 445.2103; found: 445.2104. IR (cm^{-1}): 3063, 2972, 2931, 1790, 1732, 1467, 1454, 1375, 1362, 1187, 1132, 1018, 996, 877, 784.

Transformation of the Product 4a to 7. A mixture of **4a** (169.8 mg, 0.6 mmol), $Mo(CO)_6$ (159.6 mg, 0.6 mmol), and Et_3N (999 mg, 15eq) in MeCN-H_2O (15:1, 5 mL) was stirred at 80 °C for 18 h. Afterward, the mixture was extracted twice with EtOAc (2 × 10 mL), concentrated, and the residue was purified by chromatography on silica (ethyl acetate/hexane = 1:1) to give **7** (49.7 mg, 60%).[11]

1-phenylethane-1,2-diol (**7**), mp = 53−54 °C ^{1}H NMR (400 M H_Z, $CDCl_3$): 7.24−7.28 (m, 5 H), 4.72−4.75 (m, 1 H), 4.06 (s, 2 H), 3.55−3.67 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 140.5, 128.4, 127.8, 126.0, 74.6, 67.9; IR (cm^{-1}): 3352, 3030, 2926, 1453, 1070, 1061, 1025, 888, 833, 759, 700.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra of all compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00460.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: xiaxf@jiangnan.edu.cn

Notes

The authors declare no competing financial interest.

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